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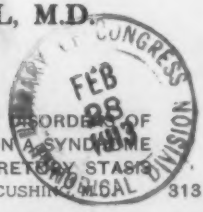

CONCERNING THE SYMPTOMATIC DIFFERENTIATION BETWEEN DISORDERS OF THE TWO LOBES OF THE PITUITARY BODY: WITH NOTES ON A SYNDROME ACCREDITED TO HYPERPLASIA OF THE ANTERIOR AND SECRETORY STASIS OR INSUFFICIENCY OF THE POSTERIOR LOBE. By HARVEY CUSHING, M.D. . . . 313

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THE

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MARCH, 1913

ORIGINAL ARTICLES

CONCERNING THE SYMPTOMATIC DIFFERENTIATION BETWEEN DISORDERS OF THE TWO LOBES OF THE PITUITARY BODY:

WITH NOTES ON A SYNDROME ACCREDITED TO HYPERPLASIA OF THE ANTERIOR AND SECRETORY STASIS OR INSUFFICIENCY OF THE POSTERIOR LOBE.[1]

By Harvey Cushing, M.D.,

PROFESSOR OF SURGERY IN THE MEDICAL SCHOOL OF HARVARD UNIVERSITY.

Introduction. It is to the credit of clinicians that our knowledge of the disorders of the various ductless glands has originated, in most instances, from studies made at the bedside. Only under the spur of these primary clinical observations have the physiologist, the morbid anatomist, and the experimental pathologist —not rarely in the person of the physician himself—been led to make their important though supplementary investigations.

Rapid as our advance has been under these combined efforts, it is to be noted that with but one or two exceptions our acquaintance with these disorders of an internal secretion is limited to those states brought about by a primary diminution, rather than increase, of functional activity of one or another of the cellular structures in question.

Thus Addison attributed the syndrome which bears his name to a destructive lesion of the suprarenal capsules; the observations of Gull and Kocher served to make clear the clinical manifestations of thyroid incompetency; tetany has become recognized as

[1] Read in the Symposium on Internal Secretions at the meeting of the American Medical Association, held at Atlantic City, June, 1912.

an expression of parathyroid insufficiency; certain forms of diabetes are associated with lesions compromising the pancreatic islets; and mutilating operations on the generative organs have long since familiarized us with the constitutional manifestations due to the deprivation of ovarian and testicular products of internal secretion, even though there remains much confusion in regard to the individual significance of the various cellular elements, interstitial and epithelial, the loss of which elicits the resultant syndrome.

In short, the recognized clinical expressions of disordered function of one or another of these structures lie on the side of secretory insufficiency, with the exception of the Graves-Basedow syndrome, in the case of the thyroid gland, and Marie's acromegaly, in the case of the pituitary body. Indeed, the latter disorder was originally ascribed to a lowered secretion, and for years futile attempts were made to reproduce the condition by glandular extirpations in animals.

Each member of the ductless gland series is doubtless susceptible, within normal physiologic limits, to a wide range both of increased and diminished functional activity; and during certain periods of physiologic stress, as in adolescence, pregnancy, and the climacteric, as well as in many conditions of disease, clinical evidences of these changes in activity may be apparent. Particularly in an individual in whom there is a tendency, inherited or otherwise, to a chemical instability of one or another of the glands, these functional fluctuations, with which we are becoming more and more familiar, in the case particularly of the thyroid gland, may overlap the pathologic so far as to give constitutional symptoms which may deserve the name of a definite malady.

With full appreciation of the close physiologic correlation of these structures—either through chemical or autonomic nervous interactions—and consequently of the polyglandular character of the syndrome aroused by a profound disorder of any individual member of the series, nevertheless there can be no doubt but that *there exists a characteristic and recognizable syndrome for a primary derangement of each individual gland, whether on the side of its secretory overactivity or of its secretory underactivity.* Furthermore, in the progress of many of these disorders, transition conditions are to be expected, and if the constitutional derangement of an earlier state, let us say of overactivity, has led to fixed somatic changes, we may anticipate clinical combinations of the opposed states, the one due to a perversion or excess of secretion and the other to a diminution or loss of secretion.

Disorders of the thyroid gland have heretofore furnished the only fairly clear example of these counterposed and transitional states, but the derangements of hypophysial function are rapidly coming to the front, for in the case of this gland also we have learned

to distinguish between the clinical evidences of an excess or perversion of secretion and those of insufficient secretion. Moreover, there are suggestions that we shall soon come to recognize clinically the constitutional effects of pathologic hyperplasia of other of these structures—adrenals, thymus, and pineal gland, as well as interstitial cells of testis and ovary—whose known disorders are now restricted to the conditions resultant upon states of insufficiency alone.

Hypophysial Disorders. In a recent presentation of some observations on a series of patients suffering from variable derangements of the pituitary body,[2] it was fully appreciated that the constitutional manifestations which were there attributed either to a secretory excess or deficit were roughly ascribed, in the majority of cases, to a disordered function of the gland as a whole. Since the gland is in reality a dualistic organ, its two lobes possessing properties of great functional divergence, it is natural that we should begin to look for clinical expressions of derangement of one or the other portion. It is this topic which I shall consider on this occasion.

Though many hypotheses have been advanced in regard to the primary pathologic lesion which incites the clinical expressions of acromegaly and gigantism—maladies whose striking phenomenon is skeletal overgrowth—it has become generally conceded not only that the overgrowth is consequent upon a hypophysial derangement, but that a functional hyperplasia of the gland is the underlying factor.

The many arguments which have accumulated in favor of this view, as opposed to the original assumption of Marie, need not be assembled here, but possibly the one which is most conclusive—though admittedly a negative argument—is that experimental ablation of a large part of the pituitary body in preadolescent animals leads to a striking failure of skeletal development. For some experiments conducted with my associates, Crowe, Homans, and Goetsch in the Hunterian Laboratory, first gave us an insight into the nature of the syndrome to which general attention was primarily drawn by Fröhlich—a syndrome in which a tumor of the hypophysis or its vicinity, in the comparatively young, is accompanied by lack of full skeletal development, by adiposity, and by the failure of full secondary sexual characteristics to appear.

Our experiments showed that these clinical states, which were immediately recognized by all as familiar ones, whether or not they were accompanied by actual tumor manifestations, were due to a hypophysial insufficiency; for many of the laboratory animals, when deprived of a large part of the gland, became obese, remained undersized, and failed to acquire their normal sexual

[2] The Pituitary Body and its Disorders, Philadelphia, 1912.

adolescence if puppies, or lost some of the attributes of adolescence if these had previously been acquired. It becomes obvious therefore that the local tumor in the clinical cases is but an incident, the effect of which has been to interfere with the gland's activity, and that the same syndrome may be expected as the result of a primary hypoplasia in the absence of tumor. This is equally true of thyroid disorders, for a tumor or enlargement of this gland, though not an uncommon accompaniment of cretinism or myxedema, is by no means essential to the process or to its recognition.

Our earlier experimental studies were directed toward the determination of the essentiality of the hypophysis to life,[3] a matter which after all is of no great moment, provided the importance of the structure to the maintenance of physiologic equilibrium is conceded; and at the time of our earlier experiments it was a general impression that the gland was of no vital importance. The experiments therefore concerned themselves largely with the effect of total or partial ablation of the gland as a whole; and in explaining the results we were led to lay too great stress on the function of the anterior lobe.

Subsequent studies conducted on another series of animals, with Goetsch and Jacobson, led to the conclusion that, apart from the growth factors, the symptoms of deficiency which we had observed were with greater probability due to an interference with the secretion of the posterior lobe—the portion of the gland which had long been shown by physiologists to contain active substances. It was found that the constitutional evidences of glandular insufficiency could be produced by the mere obstruction of the hypophysial stalk; and thus we have come to hold the view, which we believe, in spite of some controversion, to be supported by experimental as well as clinical evidence, that the secretion of the posterior lobe finds its way into the cerebrospinal fluid.

On this conception, therefore, stripping the subject of all details, the strictly epithelial portion of the gland, or *pars anterior*, is a typical ductless gland, which discharges its secretion into the large sinusoidal blood channels which traverse it. It is chiefly related to factors of skeletal development, and may be considered to elaborate a hormone capable of stimulating growth. On the other hand, the neuro-epithelial *pars posterior* is, in a sense, a gland of external secretion, its active principle or principles reaching the blood stream by way of the cerebrospinal fluid.

The posterior lobe, moreover, is closely related to metabolic processes, and particularly to the assimilation of the carbohydrates. A deficiency of its secretion, whether produced by experimental

[3] Concerning this point the interpretations of Paulesco and of Crowe, Cushing, and Homans (Bull. Johns Hopkins Hosp., 1910, xxi, 127) have been controverted by Handelsmann and Horsley (British Med. Jour., 1911, ii, 1150) and by Aschner (Arch. f. d. ges. Physicl., 1912, cxlvi), using a different operative approach.

ablation of the gland or by obstruction of the infundibular stalk, or by a pathologic lesion—tumor or otherwise—which produces a corresponding secretory loss or stasis, leads to a noticeable increase in the tolerance for sugars, with associated tendency to adiposity, a subnormal temperature, somnolence, dry skin, polydipsia, and polyuria, loss of hair, characteristic psychic, often epileptiform, disturbances, and so on—a sort of "pituitary myxedema," as it were. An excess of posterior lobe secretion, on the other hand, whether the result of some functional disorder or due to the over-administration of extracts, causes tissue waste with loss of flesh, a relative intolerance for carbohydrates, often with spontaneous glycosuria, a moist skin, etc.—symptoms, in other words, the reverse of those recounted above.

Moreover, in each case symptoms referable to a secondary derangement of other ductless glands occur, more notably on the part of the generative organs, with an apparent activation when there is hypophysial hyperplasia, and unquestioned anaphrodisia —even lack of development or atrophy—when there is hypophysial hypoplasia; and it is possible that this pituitary and gonadial relationship is more intimately a posterior than an anterior lobe effect, though this is a matter of present conjecture.

Now in our series of carefully observed examples of hypophysial derangement, which at the present writing comprises over 60 cases, it has seemed that some clinical differentiation between a disordered function of the two lobes was possible, not only in some of the patients with typical and outspoken manifestations of acromegaly —a condition ascribed to glandular hyperplasia—but in others as well who presented manifest adiposogenital dystrophy—a condition ascribed to glandular hypoplasia. Moreover, there have been a number of clinical types which have conformed neither with the typical syndrome of Marie nor with that of Fröhlich—types, as we shall see, which suggest a functional hyperplasia of one lobe with lowered activity of the other.

1. *The Acromegalic Syndrome.* On the assumption that overgrowth is related to a pathologic hyperplasia of the anterior lobe which expresses itself as more or less pronounced gigantism if the disorder occurs before ossification of the epiphyses, or as more or less pronounced acromegalic changes if epiphysial union has already taken place, it has been of interest to find that all but 3 of the 14 pronounced acromegalics of our series, at the time they came under observation, were exhibiting evidences of what we regard as a posterior lobe insufficiency. They were acquiring some measure of adiposity; they all possessed a high, often an exceedingly high, tolerance for sugars; they showed a tendency toward somnolence, a subnormal temperature, anaphrodisia, and the rest. On the other hand, in the earlier stages of acromegaly, or in periods of exacerbation of the disease, there is apt to be a reverse picture,

with an active metabolism, of which spontaneous glycosuria is a not infrequent expression.

These observations therefore suggest that a hyperplasia of both lobes of the gland occurs during the acute stages of the malady, whereas with the further advance of the disease there is a tendency at least for the posterior lobe, and possibly for the *pars anterior* as well, to undergo such retrogressive changes as to leave the structure functionally deficient.

Radiographic studies of the cranial base of all acromegalics show an enlargement of the pituitary fossa, even though the hypertrophic gland, in the majority of instances, fails to reach such a size as to produce neighborhood pressure symptoms. During the progress of the disease, however, the gland is capable of such involutional changes that it may no longer fill the enlarged fossa, and may, indeed, on chance postmortem examination, be found to present no apparent gross or microscopic abnormalities whatsoever. On this basis are easily explained the occasional reports which have been made of acromegalics who have succumbed to intercurrent diseases and in whom the hypophysis has shown no apparent deviation from what is regarded as normal—certainly no hypertrophic enlargement.

2. *The Syndrome of Dystrophia Adiposogenitalis.* In typical examples of this syndrome of Fröhlich it is natural to assume that a pathologic hypoplasia of both parts of the gland has occurred. In most of the cases heretofore recorded the lesion has been shown to be either an interpeduncular cyst containing squamous epithelial elements, or a teratomatous growth arising from an anlage related to the original pharyngeal pouch which serves to compress the gland directly.

In the typical cases, moreover, the symptoms date from a preadolescent era, and as a consequence of the anterior lobe implication the stature remains small. On the other hand, the adiposity and its allied evidences of lowered metabolic activity, which have been recounted above, indicate a coincident posterior lobe obstruction, to which, likewise, the genital dystrophy with imperfect acquirement of secondary characteristics of sex may also point.[4]

We see therefore that these two syndromes in their typical form correspond, in the case of acromegaly, with an apparent secretory activation of both lobes of the gland, at least during the early

[4] It is to be emphasized, of course, that the so-called syndrome of *adiposogenital dystrophy* may first appear in adult life when full stature has been acquired. Moreover, it need not be associated with tumor. Traumatic hypophysial lesions, for example, may lead to the same syndrome through actual glandular destruction—a condition comparable to the experimental reproduction of the syndrome in adult animals by extirpation methods. It is to be noted, furthermore, in the cases in which tumors are actually present, that adiposity with high sugar tolerance is not inevitable, for *there are lean as well as fat types of these individuals.* However, in the examples of the former which have come under our care the reproductive powers have not been impaired, despite the imperfect secondary characteristics of sex shown by absence of pubic and axillary hair, etc. The adipose types, on the other hand, have usually been impotent.

stages or subsequent exacerbations of the disease; whereas in the syndrome of Fröhlich there is a primary and chronic lowering of activity of both anterior and posterior lobes, the result of direct compression.

Now, in the production of one or the other of these syndromes it is not impossible that one lobe alone of the gland may be functionally deranged. Thus it is conceivable that the essential features of acromegalic overgrowth may be occasioned by an hyperplasia in which the anterior lobe alone participates. On the other hand, it is beyond conjecture that lesions limited in their effect to the posterior lobe may give clinical symptoms. This, as we shall see, is a particularly common sequel of hydrocephalus, but it may occur, as well, as a consequence of the very type of growth acknowledged to be a common cause of the typical syndrome of Fröhlich.[5]

In our series of cases of brain tumor, symptoms suggestive of hypophysial insufficiency have occurred with such frequency that it has become a routine of history-taking to assemble them apart from the strictly neurologic findings. Moreover, in the routine examination of fatal cases in which the central nervous system has been hardened *in situ*, it has been observed that more or less flattening—"saucer deformation"—of the pituitary body is a common finding, particularly with an internal hydrocephalus involving the third ventricle.

On the presumption that the posterior lobe of the gland discharges into the cerebrospinal fluid, hydrocephalus may be expected to cause a mechanical retention of the products of secretion of this part of the gland; and we have thus come to explain the adiposis, subnormal temperature, and high sugar tolerance which these patients often exhibit. In other words, a distant lesion with secondary ventricular hydrops is equivalent, in its effect on the posterior lobe, to the actual experimental obstruction of the hypophysial stalk or to the direct pressure of a superimposed (infundibular) tumor.

3. *The Syndrome of Overgrowth with Adiposity.* The anterior lobe, under the circumstances recounted above, may remain unaffected, as the vascular channels into which it discharges need not be seriously compromised. Under certain conditions, however, it may seemingly respond, by a hyperplastic reaction, to these pressure effects transmitted through the cerebrospinal fluid, and thus a definite acceleration of growth may accompany the

[5] We have had one straightforward example of this with postmortem confirmation. A young adult with moderate adiposogenital dystrophy and bitemporal hemianopsia showed no skeletal changes whatsoever, and the *x*-ray disclosed a normal sella turcica. The patient died from an intercurrent malady, and at autopsy a typical squamous-celled cyst of pharyngeal duct origin was found situated on the infundibular stalk well above the sella, which was of normal configuration and contained an average-sized, undeformed gland. The anterior lobe was normal, whereas the posterior lobe showed the characteristic cellular appearance of obstruction.

adiposis, increased sugar tolerance, and other symptoms attributed to the posterior lobe stasis.[6]

A notable example of this was seen in an adult patient with a large cerebellar cyst (unsuspected and found at autopsy) in whom an acute acromegaly supervened during the progress of the cerebellar lesion, which eventually led to a ventricular hydrops.[7] Doubtless the adult skeleton is relatively insusceptible to the stimulus of the hormone of growth; and so far as I am aware this is the only recorded example of the combination of hydrocephalus secondary to tumor with resultant enlargement of the acral parts of the body. In the case of the young, however, it is otherwise, and in our brain tumor series many examples of rapid growth combined with adiposity—in other words, of presumed hyperplasia of the anterior lobe with lowered posterior lobe activity—have been observed.

It is particularly important, however, that we should learn to recognize these clinical expressions of hypophysial disorder in the absence of brain tumor symptoms or radioscopic enlargement of the pituitary fossa, in the same way that it is important for us to recognize thyroid disorders unaccompanied by gross evidences of change in the configuration of the gland.

Hence the following three recent examples have been chosen to illustrate the symptom complex under discussion. The first would pass for the typus Fröhlich were it not for the overgrowth and the absence of tumor. The physical type is not an unfamiliar one.

CASE I.—*Adiposogenital dystrophy, with epilepsy and overgrowth.*

March 4, 1912. Charles H., aged ten years, admitted with the complaint of epilepsy and adiposity.

He is the eldest child; born after a prolonged labor; birth weight, fourteen pounds.

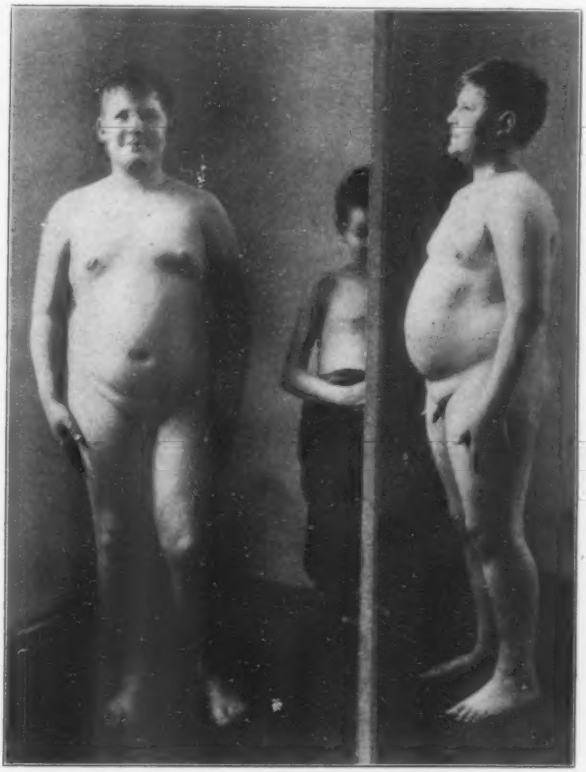
He has had epilepsy since his first year. The attacks are severe and frequent, often ten or more a day. Nevertheless, he is of average intelligence, and attends school with children of his own age, and stands well in his classes.

Following an attack of typhoid three years ago there was a marked change in his dispositional and other characteristics. From being tractable he has become an irritable and stubborn child. He has grown rapidly in height and has become very obese, though he was always large for his age.

[6] It should not be overlooked in this discussion that similar mild grades of skeletal overgrowth or incipient gigantism occurring in conjunction with adiposity have been attributed by Marburg and Frankl-Hochwart to lesions (tumors) of the pineal gland; but these cases are characterized by a remarkable precocity of adolescence, with early acquirement of secondary characteristics of sex, whereas tardy and incomplete manifestations of sexual adolescence characterize the hypophysial group. Moreover, as I have pointed out in the discussion of a case of supposed pinealism of this type, internal hydrocephalus with secondary hypophysial implication is inevitable with a pineal tumor of any size, so that a composite pineal and hypophysial glandular syndrome may be anticipated. A certain measure of *Frühreife* may occur with hypophysial lesions which are presumably primary, as in Case III of the present report.

[7] Loc. cit., "The Pituitary Body and its Disorders," Case XXXVIII, p. 194.

Physical Examination. A light-complexioned, oversized, petulant, fat boy (Figs. 1 and 2), weighing 70 kilo., or 155 pounds (normal for his age, 30 kilo., or 66 pounds), and measuring 149 cm. in height (normal average, 132 cm.). He therefore stands 17 cm. ($5\frac{3}{4}$ inches) and weighs 40 kilo. (89 pounds), more than the average boy of his age.[8]



FIGS. 1 and 2.—Case I. Overgrowth, with adiposity. Patient on left contrasted with boy of same age and average height. Weight, 155 pounds (average normal, 66 pounds).

Neuromuscular, visceral, renal, arteriovascular, and other systems negative. Blood and urine negative.

There are no definite pituitary *neighborhood symptoms*, though in some respects his attacks suggest uncinate fits. There is a slight left abducens palsy. A cranial radiogram shows a small sella

[8] Boas' tables, Science, April 12, 1895.

perched on a solid (non-cellular) sphenoidal base. The head is not large (54 cm.); there is no internal hydrocephalus.

The skeletal configuration and the disposition of the panniculus are of feminine type (Figs. 1 and 2). Circumferential measurements are as follows: over pectorals, 97 cm.; at umbilicus, 104 cm.; over hips, 99 cm.; thigh, 61 cm.; calf, 38 cm.

Aside from the overgrowth and adiposity the *hypophysial symptoms* are not very conspicuous. The skin is delicate, smooth, and hairless except for the normal growth on the scalp. The temperature is subnormal, ranging from 96° to 98°. The assimilation limit for levulose is high, 200 grams giving a bare trace of sugar in the urine. No polyuria.

There is no clinical evidence of derangement on the part of the other glands of internal secretion, except that the genitalia are abnormally small.[9]

In physical appearance this boy is the exact counterpart of another patient whose case has been reported in greater detail[10] as one of dystrophia adiposogenitalis. In both instances there occurs the same type of sella perched upon a solidified instead of the usual cellular sphenoidal base, and we have observed a similar condition in a number of other epileptics. In both cases, furthermore, the administration of glandular extracts apparently served to check the epileptiform seizures, which seemingly bear some relation to pituitary insufficiency, as has been elsewhere emphasized. Glandular therapy, however, has not so effectually overcome the tendency to adiposity in this, as it appears to have done in the patient more fully reported in my monograph.

The following two patients are physical counterparts of one another in so far as their ductless gland symptoms are concerned. One of them, however, is suffering from a primary brain tumor to which the hypophysial disorder is secondary; in the other there are no unequivocal tumor manifestations.

CASE II.—*General pressure phenomena, with secondary hypophysial symptoms, overgrowth, adiposity, sexual dystrophy.*

May 24, 1912. Leon S., aged sixteen years, a schoolboy, referred with the complaint of headaches and a possible diagnosis of pituitary disorder.

He is an only child. Until his present illness he has always been vigorous and athletic. About six years ago he received a cranial injury, followed by unconsciousness; this has left a scar on his forehead.

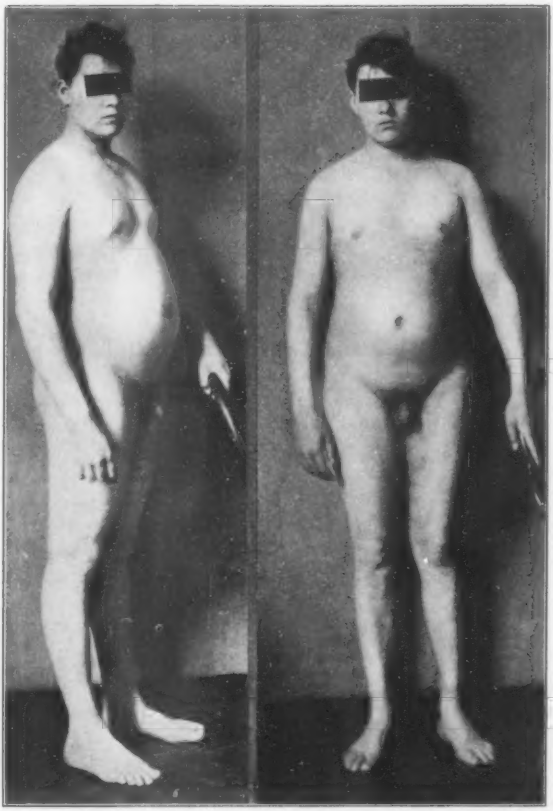
Present Illness. He began having frontotemporal headaches nine months ago. Coincidently he acquired a ravenous appetite, especially for sweets, and during the following six months his

[9] Pituitary feeding was instituted, and there have been no seizures up to the time of this writing (an interval of three months).

[10] Loc. cit., "The Pituitary Body and its Disorders," Case XXXIV, p. 175.

weight increased from 133 to 205 pounds. A rapid growth (estimated at three inches) occurred during the same period. Polyuria and polydipsia were also pronounced.

Six months ago he had a severe illness of three weeks' duration, with fever, cough, rusty expectoration, great accentuation of his



FIGS. 3 and 4.—Case II. Overgrowth, with adiposity in association with brain tumor. An increase of 2 inches in height and 72 pounds in weight in nine months.

headache, drowsiness, and stupor. There have been several recurrences of a similar nature, always with bursting headache, some delirium, and fever.

These recurring attacks, with polyuria, polydipsia, and polyphagia, and a constant increase in weight, continued until three months ago. Since that time a vigorous treatment with thyroid extract has been instituted, and under it he has lost 20 pounds.

He has become more and more drowsy, stuporous, and indifferent. His memory has become impaired, his statements are unreliable, and orientation for time and place seem uncertain. There have been periods of diplopia. He has had hallucinations of sight and sound; and hiccoughing, nausea, and vomiting have accompanied the more severe recent headaches.

Physical Examination. An overgrown, abdominous boy, with a peculiar grayish, edematous-looking, and almost hairless skin. Temperature and pulse slightly elevated. Blood pressure 110. Visceral (cardiovascular, thoracic, and abdominal) examination negative. Blood (Wassermann), cerebrospinal fluid, and urine negative.

Symptoms of intracranial tension are pronounced. Aside from the headaches and vomiting there is a choked disk of 3 D. on the right and 2 D. on the left. The *neurologic examination* shows, further, a weakness of the left abducens, increase in the deep reflexes throughout, with ankle clonus and a positive Romberg sign. Psychic disturbances are profound, with loss of memory, extreme drowsiness, apathy, and some disorientation. The cranial röntgenogram shows large diploëtic channels and slight separation of the sutures characteristic of internal hydrocephalus.

Analysis of Hypophysial Symptoms. (*a*) *Neighborhood:* The sella is of normal outline, possibly slightly enlarged (1.4 cm. by 0.8 cm.). There are no local pressure disturbances.

(*b*) *Secretory.* The body configuration is of a feminine type, with broad hips, genu valgum, and tapering extremities. Height is 170.6 cm. (5 feet 7⅛ inches). Circumferential measurements: thorax, 96 cm.; abdomen, 98 cm.; hips, 106 cm. (Figs. 3 and 4).

Cutaneous. The skin shows a peculiar, cadaverous pallor, though the blood gives 86 per cent. of hemoglobin. Its appearance is not unlike that in cases of nephritis with edema. It has a slightly more yellowish tinge, however, than in some of the pronounced cases of hypopituitarism that we have seen. It is soft, fine, and delicate. There is a slight axillary moisture, but the extremities are exceedingly dry.

Hirsuties. With the exception of the scalp and a slight growth of hair with feminine distribution on the pubes, the body is hairless. The patient has never shaved.

Subcutaneous. The fat is abundant, particularly over the hips, thighs, and pectorals. It is tender, even on slight pressure ("adiposis dolorosa"). There is some pigmentation around the neck in the axillæ, and between the symphysis and umbilicus is a pigmented line similar to that seen in pregnant women. There are many lineæ atrophicæ over the hips.

Polyuria and polydipsia were formerly marked symptoms. Pulse and respiration are not subnormal—indeed, there is a slight elevation. Blood pressure, 110. Apathy, drowsiness, and stuporous

periods are characteristic features. *Sugar tolerance* is not determinable, as amounts of levulose over 150 grams cannot be retained.

Other Ductless Glands. Adrenals: Asthenia and pigmentation. Thymus: Some increase in retrosternal dulness, extending about 4 cm. to the left of the sternum and over the first interspace at the right; no lymphatic enlargement. Testes: Decidedly smaller and softer than normal.

Diagnosis. Brain tumor, possibly cerebellar, with low grade of internal hydrocephalus and secondary functional pituitary disturbances.

Operation. June 1, 1912. Right subtemporal decompression. Subsequent lowering of choked disk to 1 D., with considerable improvement in other respects. Patient discharged June 20.

The clinical picture in the following case is very similar, so far as the growth and adiposity are concerned, though in this instance there are no certain tumor manifestations.

CASE III.—*Overgrowth, adiposity, hypertrichosis.*

June 7, 1912. Donald S., aged sixteen years, admitted with the complaint of overgrowth, lowered mentality, and adiposity.

Family history without record of abnormalities, unusual stature or corpulence.

Personal History. A normal, ten-pound, breast-fed baby. Has had measles, chickenpox, and mumps. Always somewhat overlarge for his age. Otherwise normal in all respects until his ninth year. Regarded as a bright and intelligent boy, in advance of his age, at school.

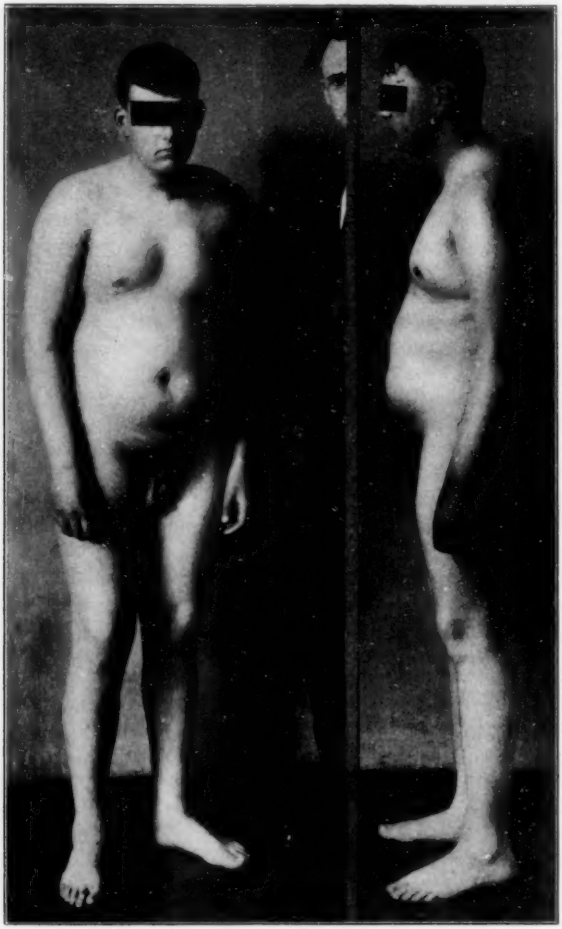
During his eighth year he acquired an abnormal appetite and became exceedingly adipose. His abdominal panniculus at this time is said to have been enormous.

At eleven years of age he was a foot taller than his contemporaries, and weighed 168 pounds (normal average, 72 pounds). At twelve years his external characters of sex were those of an adult, but he has never shown any sexual instincts; no priapism or pollutions.

He was sent to a strict military academy, where in the course of a year an attempt was made to reduce his weight by excessive physical exercises. His parents and teachers attributed his condition to overeating; and, being much abused and teased by his schoolmates as a "stupid fat boy," he became depressed and melancholy. Though kept at school, there has been but little mental advance in the past two years; he shows no initiative faculties, "behaving in many respects like a boy of six."

Polyuria and polyphagia, with an abnormal appetence for sweets, extensive drowsiness, constipation, and sensitiveness to cold, have been marked features. Occasional attacks of vomiting have been attributed to overfeeding. There has been no headache.

Physical Examination. Practically negative except for the psychic conditions and signs attributed to disorder of internal secretion. Temperature markedly subnormal, often 97°. Pulse slow, often 60. Blood pressure variable, often below 100.



FIGS. 5 and 6.—Case III. Overgrowth, with adiposity. Height of patient on left, aged sixteen years, contrasted with that of father.

Mental Status. Memory poor; feeble powers of initiation and concentration; inattentive, irritable, morose. Speech hesitating, stuttering, and disconnected; responses slow, frequently irrelevant.

He falls asleep at any and every opportunity. Occasional involuntary twitchings of face and hands. He has a peculiar mania for writing inconsequential letters to people. *Neurologic examination* otherwise practically negative. No general pressure symptoms, though the optic disks are slightly congested. Pupils are irregular, with sluggish reactions and a coarse horizontal nystagmus, more marked to the left. There is a peculiar ataxia in his gait, which may be of cerebellar origin.

Analysis of Hypophysial Symptoms. No neighborhood disturbances. The sella is of small size (0.8 by 0.7 cm.), but shows no abnormalities; sphenoidal cells unusually large and extend into the dorsum sellæ.

Skeletal Configuration. Height, 173.5 cm. (5 feet 8¼ inches, or 3¼ inches above the average), despite a marked dorsal kyphosis. Usually large frontal sinuses, but otherwise no cranial abnormalities; circumference, 56.5 cm. Eyes deeply set; dental arches narrow; second teeth small but well formed. Limbs long and tapering. Extremities large; wears an 8½ shoe. Circumference of thorax, 98 cm.; of hips, 102 cm. There is a suggestion of typus femininus; slight genu valgum (Figs. 5 and 6).

Cutaneous. Skin is soft and dry. Extremities dusky and cyanotic. Many purplish lineæ atrophicæ. Definite hypertrichosis. Hair abundant in zone around upper sacral level, over extremities, pubes, and axillæ. Pubic growth since twelve years of age. There is some hair on chin and lips; has shaved at intervals for the past year. Eyebrows heavy.

Adiposity marked, with considerable tenderness on pressure. At eleven years patient weighed 168 pounds; present weight, 178 pounds (Boas gives the average as 110). Special accumulations of fat over abdomen, hips, pectoral regions, and inner aspect of thighs.

Metabolic activity low (*cf.* polyphagia, adiposity, subnormal temperature, etc.). Levulose assimilation limit, 250 grams.

Other Ductless Glands. Thyroid small; isthmus barely palpable. Thymus, pancreas, and adrenals negative. Testes normal; scrotum lax. Penis undeveloped (*cf.* early acquirement of secondary characters without development of sexual instinct).

June 10. Discharged, taking pituitary tablets.

Though these patients exhibit a syndrome of adiposogenital dystrophy, it is apparent that in some essential features they fail to conform with the type of Fröhlich.

Doubtless these disturbances of growth and metabolism would never have been credited with any possible alliance with a ductless gland disorder, and particularly with an hypophysial disorder, were it not for the fact that corresponding syndromes occur when the gland's activity has obviously been implicated in one way or another in association with a gross lesion of the neighborhood.

Fortunately, both in maladies associated with skeletal overgrowth or dwarfism and in those accompanied by excessive adiposity with genital derangement, pituitary hypertrophies, tumors or cysts, have been found often enough to justify us in attributing similar clinical pictures to a corresponding secretory change in the absence of a local neoplasm.

In varying grades the type is doubtless a common one, more or less familiar to all. One need but recall the fat boy depicted in "The Pickwick Papers," whose employment with Mr. Wardle consisted in alternate eating and sleeping. The combination of drowsiness, inertia, and an excessive appetite is often merely an expression of metabolic inactivity due to ductless gland insufficiencies.

Conclusion. The view is advanced that skeletal overgrowth, possibly combined with certain cutaneous changes and hypertrichosis, is an indication of anterior lobe hyperplasia. On the other hand, certain types of adiposity with an increased assimilation limit for carbohydrates, often with dry skin, subnormal temperature and pulse, are characteristic of the metabolic disturbances from posterior lobe insufficiencies. Hypotrichosis and sexual dystrophy are common accompaniments.

Assuming the combination of these factors, certain not unfamiliar clinical syndromes, in which overgrowth is associated with adiposogenital dystrophy, can be explained. They differ from the accepted syndrome of Fröhlich not only in the absence of an hypophysial tumor with sellar enlargement, but also in their opposed skeletal features.

These physical states, in brief, are interpreted as the expression of an anterior lobe hyperplasia combined either with posterior lobe hypoplasia or with what is in effect the same thing, stasis of posterior lobe secretion.

GASTRIC DISTURBANCES IN TABES DORSALIS.

By William Fitch Cheney, M.D.,

Clinical Professor of Medicine, Leland Stanford Junior University Medical Department, San Francisco, California.

During the past year the writer has observed five patients who presented themselves because of gastric disturbance, in whom this ultimately proved to be but one of the manifestations of tabes dorsalis. None of these patients had previously been made aware of the real nature of their disease, though all had been suffering for years. Two had been operated upon for supposed gastric ulcer, without the slightest relief of their symptoms; and a third was also subjected to surgery, by the advice of the writer, before

the fact was discovered that no organic disease of the stomach existed and the real situation was disclosed. All these facts seem to indicate that the gastric manifestations of tabes are not always recognized as promptly as they might be, and that perhaps more cases of "stomach trouble" are in fact spinal in origin than is generally realized.

The first case to be reported is a particularly remarkable one because of the unusual association of hematemesis with the gastric crises.

CASE I.—T. Y., a Japanese, aged thirty-four years, was first seen in September, 1911, complaining of stomach trouble.

History: For seven years he had had recurring attacks of abdominal pain, with vomiting. These came at irregular intervals. Between times he felt perfectly well. During 1910 he had two severe attacks. In 1911 the last one came about five weeks before we saw him first, and he had then been in the hospital for three weeks. Previously to that he had been at work and feeling well.

The pain was always felt in the pit of the stomach; did not radiate from there; was very severe; in character was described as a "shooting pain;" came on without reference to food taken; frequently began in the night, arousing him from sleep; lasted for several days without relief. Vomiting was constant while the pain lasted, but did not give relief. Taking food made no difference one way or the other, but no food was retained or desired. With his last attack he had vomited blood, but never before.

Physical Examination: The patient was a well nourished man, apparently well. No abnormality was found in heart, lungs, liver, or spleen. The abdomen showed slightly greater fulness and rigidity in the left hypochondrium than in the right, but no tenderness over the stomach; no palpable mass; no succussion splash; no peristaltic wave; no evidence of dilatation or of pyloric obstruction. The patient pointed always to the lower end of the ensiform as the site of his pain.

Gastric Analysis: One hour after the Ewald test meal four ounces of contents were removed, not well triturated, showing a little blood, much thick, ropy mucus, a few chunks of meat, and considerable butter, retained from the previous meal six hours before. Total acidity, 48; free HCl, 16; combined HCl, 16; organic acids and acid salts, 16.

TREATMENT. The patient was advised as to his diet, excluding all coarse and irritating foods, but was given no medicine. He remained perfectly well for two months following.

Recurrence: On November 29 he returned to Lane Hospital, because the previous afternoon he began suddenly and without warning to have violent pain in his stomach, and to vomit blood. In spite of withholding all food by mouth, applying an ice-bag over the stomach, and giving morphine hypodermically, he con-

tinued during November 29 and 30 to have violent pain and to vomit repeatedly, the vomitus being a brownish, bloody fluid, containing numerous shreds and flecks of brownish or reddish material which responded to all tests for blood. After two days the vomiting and pain suddenly ceased, and he was able to take food.

OPERATION. Convinced after witnessing this attack that there must be some serious organic disease of the stomach, most probably ulcer, we advised exploratory laparotomy. This was done by Dr. Stanley Stillman on December 9, but no abnormality of any kind was found in stomach, duodenum, gall-bladder, liver, or appendix, and the abdomen was closed without anything done but exploration. Except for another violent attack of pain and vomiting, with the same character of bloody vomitus as before, shortly following the operation, the convalescence was uneventful.

Further Recurrence: On April 16, 1912, the patient was again brought to Lane Hospital from his home in the country. Following his operation he remained well and gained in weight. On the evening of April 15 he began again to have a violent paroxysm of pain and vomiting, vomited all night, and the same bloody material as before. Seen at 9 A.M. on April 16, he was retching violently, and had brought up in repeated small amounts about eight ounces of a dark brownish material, with much mucus, plainly bloody. He continued to have pain and hematemesis for three days, when the attack abruptly ceased.

Spinal Fluid: On April 19, 5 c.c. of spinal fluid were obtained by lumbar puncture. This showed a faint opalescence on boiling; positive Nonne reaction; negative Noguchi; sixty lymphocytes in 1 c.mm., and no polymorphonuclears; a positive Wassermann reaction in all dilutions.

Evidence of Tabes. Further physical examination now elicited the following facts:

Pupils: The right was regular in outline, the left was slightly irregular, and both reacted incompletely and sluggishly to light.

Abdominal reflex was present and lively on both sides, likewise the cremasteric.

The plantar, achilles, and patellar reflexes were completely missing on both sides.

Sensation was diminished over the legs from the knees down to heat and cold and to pain, but not to touch; the patient swayed when standing with eyes closed, and had to be supported or he would have fallen; he walked clumsily and stumbled, but his gait was not definitely ataxic.

Subsequent History: On April 29 the patient was given 0.6 gram of salvarsan intravenously, and a prescription containing bichloride of mercury and iodide of potassium for regular use by mouth. In spite of this treatment he had another attack in May

and another in June; he then returned to Japan, and we have had no further report of his condition.

A case similar to this forms the subject of one of Charcot's lectures in his *Lecons du Mardi*.[1] He speaks of hematemesis, "vomissements noirs," as a rare feature in gastric crises, and says that besides this case of the patient he is presenting he knew of but one other, previously reported by Vulpian. But that was in 1889. Oppenheim,[2] in the latest edition of his text-book on nervous diseases, mentions hematemesis as a rare occurrence in gastric crises, but refers to observations of it by Vulpian, Charcot, von Noorden, Eckert, Rubin, Neuman himself, and Von Jappa[3] reports a case of gastric crises associated with hematemesis during one recent attack, but not with any other previous, though they had recurred at intervals for six years. At autopsy this patient was found to have not only characteristic spinal changes, but in the stomach the scar of a gastric ulcer, with an eroded vessel. Von Jappa questions whether in such a case the gastric ulcer is simple accidental coincidence or is a mucous membrane defect secondary to trophic disturbance from tabes. He agrees that it is possible to have pure parenchymatous bleeding in gastric crises, without ulcer, and such was the condition in the case of the Japanese just reported, for the stomach was examined carefully at the operation and no ulcer was found. Ranzier and Roger[4] have also recorded the history of a case of severe gastric crises, ultimately accompanied by hematemesis, and closely resembling gastric ulcer. Probably as more such cases are put on record, and attention is called to the possibility, the correct interpretation will more frequently be made previous to laparotomy.

Case II.—A Scotchman, aged forty-one years, was first seen in the medical ward of Lane Hospital in October, 1911. He complained of attacks of pain in the pit of the stomach, with nausea and vomiting, recurring for two and a half years past; though he had had "stomach trouble"—sour eructations and belching after eating—for ten or twelve years before that. His severe attacks were frequent, with only a few days intermission, and they lasted only for one day or sometimes for three or four. They seemed to have no relation to the taking of food. They came on suddenly, with sharp, cutting pain in the pit of the stomach, nausea, and repeated vomiting. He had never vomited any blood nor passed any by bowel. Three months before coming to the hospital he had had his abdomen opened, but was told that nothing was found, and his attacks persisted afterward as before.

[1] Charcot, Oeuvres Completes, ii, 331.
[2] Fünfte Auflage, S. 174.
[3] Ueber Bluterbrechen bei gastrischen Krisen, Inaug. Dissert., Berlin, 1911.
[4] Crises gastriques subintrantes avec hematemesis au cours d'un tabes fruste, Montpellier Méd., 1911, No. 41.

This patient was found[5] to have inequality of his pupils, the right being markedly larger than the left; neither pupil reacted to light, and the left only slightly to accommodation, the right not at all. The left Achilles tendon reflex was absent, but the right was lively; the corneal reflex was absent in both eyes; but all other superficial and deep reflexes were normal. Hyperesthesia to heat and cold, with hypoesthesia to tactile irritation, was found over both lower limbs from knees to hips, and continuing over the trunk posteriorly as high as the angles of the scapulæ, but extending anteriorly only as far forward as the nipple line on each side, leaving the abdominal wall above Poupart's ligaments apparently normal in its sensibility.

There was a positive Wassermann reaction in the blood and in the spinal fluid, and the latter showed 20 cells per cubic millimeter, all lymphocytes. The stomach showed hypersecretion not only after the Ewald meal but also in the fasting state, in the early morning.

This patient twice received salvarsan intravenously, with the result that his gastric crises occurred much farther apart afterward, and were briefer in duration, but they did not entirely cease.

Case III.—A Japanese, aged twenty-eight years, entered the medical ward at Lane Hospital in January, 1912, complaining of stomach trouble. During the year and a half previous he had had four or five similar attacks. The present attack began four weeks before. The characteristic feature of this case was vomiting; at the outset he vomited for four or five days every fifteen minutes without stopping, then for two days he did not vomit at all; since then he had vomited several days at a time quite frequently, with intervals of several days with none. He also complained of pain, burning in character, up and down the anterior surface of the trunk, from throat to navel, present continuously for five weeks. No previous attack had ever lasted over two weeks.

This patient showed loss of both patellar and both Achilles reflexes, but no other evidences of tabes. His blood and spinal fluid both showed positive Wassermann reaction, and the spinal fluid contained 26 lymphocytes per cubic millimeter.

After salvarsan intravenously his condition was much improved, and his vomiting and pain gradually ceased, but his subsequent course could not be followed.

Duration of Gastric Crises. The two cases just described bring up the question of possible duration and frequency of gastric crises in tabes. The ordinary course is that noted in Case I. Attacks come at intervals of two or three months and last for three days to a week, repeating themselves throughout three to

[5] In the neurological examination of this and of the subsequent cases I have had the coöperation of Dr. W. F. Schaller, instructor in neurology in Stanford University, Medical Department.

six years. But Charcot, in his description of the possible variations from type, mentions gastric crises that occur with great frequency, even daily, but lasting for only four or five hours; while, on the other hand, the length of the crisis, in place of three, four, or five days, as in the typical condition, may be extended to fifteen or twenty days, a month, or even more, while at the same time the intervals shorten. Thus the gastric disturbances of tabes may even establish themselves as more or less of a permanency, without cessation or intermission, for a period of many months.

CASE IV.—An Irish laborer, aged forty-seven years, was first seen in October, 1908, complaining of stomach trouble. For six or seven years before he had had recurring attacks of the same sort, at first with several months' interval, but gradually growing more frequent. They were characterized by nausea, belching, vomiting, but no intense pain, only a gnawing, distressed feeling. Such attacks always lasted only a week or two, and in the interval he always felt well. During an attack all food increased his distress, and he feared to eat. Vomiting came on because of the discomfort, and usually relieved it. He had never vomited any blood. The present attack, that brought him for advice, was the most severe he had ever had. His stomach was found dilated, but there was no palpable tumor over it and no tenderness. The contents gave a total acidity of 100 and free HCl 60. The case was only seen for diagnosis at that time, and was not understood, though ulcer was suspected.

The man was not seen again until August, 1912, when he returned for advice about pains in his chest. Subsequent to his previous visit he had no further attack of his stomach trouble for two years, and then only a mild recurrence, and after that no more at all. In February, 1912, he began to have dull pain in his lower limbs, from his knees down, like rheumatism, but could stand or walk without increase of pain. Suddenly the pain left his lower limbs and went up into his abdomen and back; it was felt around the trunk, particularly over the abdomen, but less severely in the back; the abdomen was tender to touch, he said, in the region where he felt his pain. Since this pain began he had lost twenty to thirty pounds in weight, and had become so weak he could hardly move around. Examination showed that over the back, between the sixth and tenth thoracic vertebræ, he had a definite area of hyperesthesia to touch or pressure, but not to pin-prick or heat or cold; evidently due to an inflammation of meninges and nerve roots in his lower dorsal region. In his lower limbs from feet to knees he also showed a disturbance of sensation, inability to distinguish heat from cold, and pin-head from pin-point. The right pupil was smaller than the left, fixed, and did not react to light; the left reacted to light, but sluggishly. There was no loss of plantar or patellar reflexes, but the Achilles was less on the right

than on the left side. The blood and the spinal fluid both gave a positive Wassermann reaction, while the spinal fluid showed also a positive Nonne and a positive Noguchi reaction, and 20 cells to the cubic millimeter.

This case brings out several points long ago emphasized by Charcot and since by others, but apparently not yet thoroughly appreciated in diagnostic work. (1) The gastric crises of tabes occur most often in that early period of the malady before motor ataxia has yet appeared, the pre-ataxic period. This phase may continue for years before locomotor troubles show themselves, and during this time the crises may be the sole manifestation of the spinal disease. This absence of other recognized symptoms of tabes in association with the gastric attacks no doubt often misleads the physician and makes him fail to understand the real nature of the condition. But even during this pre-ataxic stage there may be minor signs of whose existence the patient is totally unaware, such as slight inequality of the pupils or a fixed pupil that does not react to light, or an absent reflex in knee or Achilles tendon, or an area of disturbed cutaneous sensation. Lumbar puncture and spinal fluid also now afford valuable aids to diagnosis, even in the pre-ataxic stage. (2) As the other symptoms of locomotor ataxia appear and progress, the gastric crises are likely to cease spontaneously, and after having suffered from them for years, the patient may finally be freed from them entirely, as the evidences of ataxia and motor incoördination appear upon the scene. (3) There are incomplete and atypical gastric crises, "formes frustes," as Charcot called them, of which this case forms an example, for the usual violent pain was lacking from his attacks. In another case it may be the vomiting that is lacking, while pain in the epigastrium is acute and prostrating. Other possible deviations from the usual type, as regards frequency of repetition of the attacks and as regards duration, have been mentioned in commenting on Cases II and III.

Case V.—K. M., a Japanese, was first seen in July 1912, complaining of stomach trouble. About seven years before he commenced to have attacks of severe pain in the stomach, but without vomiting. Six years before he had been operated upon in the country, the abdomen opened, and the stomach explored. He did not know what was found, but his attacks continued after the operation just the same. Later on these attacks consisted of vomiting and diarrhea as well as of pain. Such attacks lasted for three or four days, he said, and recurred irregularly every few months. The one observed in July, 1912, included very violent epigastric pain, repeated and violent retching, inability to retain any nourishment, many bowel movements each day, apparently without cramps, considerable prostration; the whole illness lasted four days; he said there had been none before for five months. He

recovered from it quite suddenly, and after it ceased was at once hungry and able to eat. The stomach was not dilated nor tender nor abnormal in contour. The contents showed no free or combined HCl, and a total acidity of but 16. The right patellar reflex was much less active than the left; the left Achilles reflex was absent entirely; there was no abnormality of the pupils. The spinal fluid showed 14 cells per cubic millimeter and a positive Wassermann reaction.

It seems remarkable that 3 out of these 5 patients observed have been Japanese. They constitute a small proportion of our material in San Francisco, and the frequency in this race of gastric crises as well as of other manifestations of tabes and of syphilis of the nervous system makes us suspect that they must be inadequately treated in their own country at the time of their initial infection.

SUMMARY. The recognition that certain gastric disturbances are really due to tabes is never difficult if one is alert to the possibility. There is no fixed unchangeable rule about the nature of these disturbances, or about their duration, or their frequency of recurrence, to make their diagnosis easy. They are not accompanied by the evidences of organic disease in the stomach that one expects to find; they recur in spite of treatment of all kinds directed to the stomach, even in spite of laparotomy; they usually appear abruptly, without reason, and cease suddenly regardless of treatment, leaving the patient perfectly free from gastric disturbance in the intervals. On the other hand, no manifestations of "locomotor ataxia" may be present for years during which the stomach upsets continue, and the patient may make none of the complaints that one expects to hear when spinal disease exists. The proof of the connection between the gastric disturbance and the spinal lesion, therefore, must often depend upon the discovery of signs of tabes of which the patient is unaware—such as faulty reflexes and cutaneous sensibility, and changes in the spinal fluid obtained by lumbar puncture; while the demonstration that active syphilis exists, by the Wassermann reaction in the blood and spinal fluid or even in the latter alone, adds the last link to the chain.

THE LYMPHOCYTOSIS OF INFECTION.

BY RICHARD C. CABOT, M.D.,

CHIEF OF WEST MEDICAL SERVICE, MASSACHUSETTS GENERAL HOSPITAL, BOSTON.

THE great majority of infectious diseases are accompanied during their acute stages by increase in the polynuclear leukocytes. A few, like typhoid and malaria, show no marked change

of any kind. *Occasionally infections usually associated with polynuclear leukocytosis show instead an increase of lymphocytes.* This was noticed many years ago by Ehrlich, and attributed by him to a passive drifting of lymphocytes out of the lymph glands and contrasted with the active emigration of the polynuclear leukocytes. Most writers have not agreed with this interpretation, but a number have noticed the occurrence of the phenomenon to be explained. It is most striking and has been most often commented upon in connection with whooping cough, where it is so constant as to be believed by some to be of value in differential diagnosis of that disease.

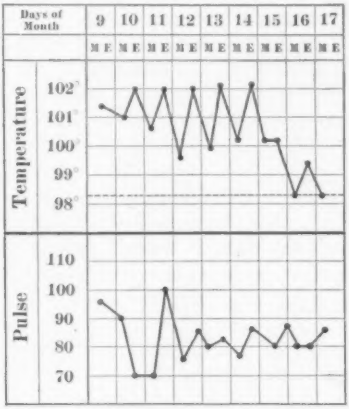
The group of cases to which I wish to call attention are such as would ordinarily be associated with polynuclear leukocytosis. They appear to be connected, at least in some cases, with a streptococcic infection, and their practical interest to clinicians arises from the fact that they are liable to be confused with lymphatic leukemia and thus to cause an unnecessary alarm as to the prognosis.

CASE I.—*Wound infection at autopsy; lymphangitis and adenitis; lymphocytosis; continued fever; recovery.* About fifteen years ago a young physician acquired a hang-nail infection at an autopsy, the nature of which I do not know. This was followed by a mild lymphangitis extending up the arm, with enlargement of the axillary glands both on the corresponding side and to a lesser extent in the other axilla. There was continued fever for several weeks, with marked prostration, the case somewhat resembling typhoid fever. The blood showed throughout a well-marked absolute and relative lymphocytosis, such that the physician himself and other consultants were seriously alarmed as to the possibility of lymphatic leukemia. The record of blood counts was unfortunately not kept, but if my memory serves me the percentage of lymphocytes never rose above 70 and the total count of leukocytes never above 20,000. The lymphocytes were mostly of the smaller types, and there were no other changes in the blood. Recovery was rather slow, but complete. This physician has had no such attack since that time, and has remained in good health.

CASE II.—*Boils; persistent lymphocytosis; recovery.* A college undergraduate, aged twenty years, was seen November 15, 1909, on account of persistent boils, which had been present for six weeks. At the start of the illness there was said to have been bile in the urine and a slight yellowish discoloration of the conjunctivæ. He had been considerably run down at the time of the onset of these symptoms, losing much sleep and working very hard.

When I saw him he was already considerably better, but still had one or two large boils freely discharging. The chart for part of the week preceding and following the time when I saw him is subjoined herewith. November 15 his blood showed: red cells,

5,180,000; white cells, 3,400. Differential count showed polynuclears 18 per cent., lymphocytes of various types 82 per cent. One of the lymphocytes was in karyokinesis, and several showed nuclei in various stages of division. Most of the lymphocytes were small, but some had the characteristics of Türck's "stimulation forms."



Temperature chart of Case II.

November 16 the polynuclears were 21, lymphocytes 79.

November 19 the total leukocytes were 16,400, polynuclears 14 per cent., lymphocytes 86 per cent. In the meantime the boy was rapidly recovering, and showed practically no symptoms.

November 20 the differential count still showed polynuclears 14 per cent., lymphocytes 86 per cent., with an increase in the total number of leukocytes estimated at 15,000.

November 23 he went home for his vacation, and after his return, December 1, was perfectly well.

Case III.—In the middle of a raging epidemic of streptococcic sore throats during January, 1912, a girl, aged twenty years, began to have a disagreeable morning headache. A week later lumps appeared under the right arm. A week later, February 3, she began to have a severe sore throat, with a temperature of 102°, lasting about four days, and accompanied by swellings in each side of the neck. During the following two weeks she had frequent night sweats. The swelling of the glands in the axilla continued and a gland became enlarged under the chin. After the fever left her she began to cough and continued to do so for three weeks, the sputum being sometimes slightly blood-streaked. With the decline of acute symptoms she continued to lose weight, strength, and color, and had a good deal of digestive disturbance.

February 16 her cervical glands, both lateral and posterior, were enlarged to the size of marbles, and in the right axilla there was a gland the size of a small hen's egg, with smaller ones in the left axilla. Glands in both groins were also demonstrably larger than the average. The spleen and liver were not felt; chest and abdomen negative, except for an abnormally dull percussion note in both apices, especially the right, and over the upper part of the sternum. The glands showed no signs of breaking down. The blood showed: total leukocytes 9000. Of these there were polynuclears 28 per cent., lymphocytes 71 per cent., eosinophiles 1 per cent.

She was seen again February 23, and was, on the whole, much better. The fever and sweating had altogether ceased, and all the glands were smaller, but still abnormal. The blood at this time showed: red cells, 5,600,000; white cells, 3600; of which there were polynuclears 36 per cent., lymphocytes 62 per cent., mast cells 2 per cent. She made an uninterrupted recovery from that time on.

Case IV.—A man, aged thirty-seven years, had what he called "a cold" in February, 1912.

March 9 he had a severe attack of vertigo while in a barber's chair, but recovered in a few minutes and has had no more such attacks since. A certain amount of cough left over from his cold bothered him a good deal during March.

March 18 he awoke with glands in the left side of his neck, sore and swollen. After three days these glands subsided, but he began to have fever which on March 22 reached 101°. For the next ten days he was in bed, with slight evening fever and night sweats.

March 28. The blood examined by the attending physician showed 30,500 leukocytes, and the counts thereafter were as follows:

		Polynuclear.	Large lympho-cytes.	Small lympho-cytes.	Eosinophiles.
March 28	30.500	25 per cent.	67 per cent.	8 per cent.	
April 5	18,900	28 per cent.	58 per cent.	20 per cent.	
April 12	26,800	50 per cent.	8½ per cent.	41½ per cent.	½ per cent.
April 15	12,500	65 per cent.			
April 20	26,700	60 per cent.	15 per cent.	24 per cent.	¾ per cent.
April 27	14,500	51 per cent.	6 per cent.	41 per cent.	1½ per cent.
May 4	19,400	55 per cent.	13 per cent.	30 per cent.	2 per cent.
May 11	15,400	56 per cent.	4 per cent.	38 per cent.	1½ per cent.
May 18	18,800	57 per cent.	7 per cent.	35 per cent.	½ per cent.

I first saw the patient May 23. At that time he was much better, but the glands were still slightly enlarged in his neck. He had no more fever and was free from night sweats, although his cough continued to some extent in the morning, and unless he stayed out of doors most of the day his temperature in the afternoon rose to 99.5° or less. Physical examination on May 23 was negative. The white cells were then 8200, polynuclears 56

per cent., lymphocytes 42 per cent.; of these 38 per cent. were of the small type, eosinophiles 2 per cent. His recovery thereafter was uneventful.

In the differential diagnosis between streptococcic adenitis, tuberculous adenitis, and lymphoid leukemia the most important point is the evidence of a cause for the adenitis, the course of the disease, and the percentage of lymphocytes in the differential count. Although this percentage is obviously much elevated, both absolutely and relatively in the cases reported here, it is considerably lower than the percentages usually seen in cases of lymphoid leukemia at that period of disease in which the patients feel sick enough to consult a physician. The majority of leukemic cases have over 90 per cent. of lymphocytes, and show in addition to the relatively well-formed cells many broken and partially decolorized remnants of leukocytes. I saw none of these broken cells in any of the cases above described.

In Case III, tuberculosis (pulmonary and glandular) had to be considered, on account of the three weeks' cough, the blood-streaked sputa, the fever, night sweats, loss of weight, and dulness at the pulmonary apices. Only by the course of the disease could tuberculosis be excluded, though the sudden onset of the symptoms in the midst of an epidemic of streptococcic sore throats made the balance incline toward septic rather than tuberculous infection.

It should be noted, moreover, that acute lymphoid leukemia often begins with symptoms like those present in Case III, and is sometimes associated with sore throat due to leukemic infiltration of the tonsillar ring.

In connection with the second of these cases I should like to call attention to the fact that an adenitis apparently originating in tonsillar infection, involved not only the cervical but axillary glands. In other such cases I have known suppuration in an axillary gland and isolation of pyogenic streptococci from the pus.

In 3 of the 4 cases here reported there is reason to believe that a streptococcus was the infecting agent. The fourth may have been of similar origin though no cultures were taken.

SUMMARY. 1. Wound sepsis, boils, and widespread streptococcic adenitis of tonsillar origin may be accompanied by a lymphocytosis so pronounced as to suggest lymphoid leukemia.

2. No reason is known for this substitution of lymphocytosis for the usual polynuclear leukocytosis of infection.

3. The distinction between such a lymphocytosis (accompanying a widespread adenitis) and leukemia depends upon the recognition of an infectious origin for the adenitis, upon the lesser degree of lymphocytosis in the infectious type, and upon the course of the disease.

GASTRIC ULCER WITHOUT FOOD RETENTION: A CLINICAL ANALYSIS OF ONE HUNDRED AND FORTY OPERATIVELY DEMONSTRATED CASES.

By Frank Smithies, M.D.,

GASTRO-ENTEROLOGIST TO THE MAYO CLINIC, ROCHESTER, MINNESOTA.

To July 1, 1912, there had been 1341 operations performed for ulcer of the stomach and duodenum at the Mayo Clinic. Of this number, 404 were proved to be ulcers of the stomach. In 264 (65.3 per cent.) of these gastric ulcers there was definite food retention demonstrable after twelve hours by the raisin and cooked-rice test (Strauss, Hansmann). In 140 (34.6 per cent.) of these operatively proved gastric ulcers no food retention was evident.

The diagnosis of surgical gastric and duodenal ulcer *with* food retention is comparatively simple, but the recognition of gastric ulcer when the stomach's emptying power is still unimpaired offers much greater difficulties. While careful development of the history, routine physical examination, and scrutiny of test-meal and laboratory data frequently admit of tentative diagnosis of gastric ulcer, a large number of cases present a picture so blurred by duodenal, gall-bladder, and appendix manifestations that unreserved diagnosis is rare.

This report has been made in the endeavor to determine the possibility of exact prelaparotomy diagnosis of the above-mentioned group of cases.

Material. The analysis covers 140 cases of proved gastric ulcers, without food retention, from the services of W. J. and C. H. Mayo.

Age. Table I indicates that the largest number occurred between thirty and forty years of age (27.2 per cent.); 92 per cent. of all cases were between the ages of thirty and sixty.

Table I.

Age.	No. of cases.	Per cent.
0 to 10	0	0.0
10 to 20	0	0.0
20 to 30	21	15.0
30 to 40	38	27.2
40 to 50	31	22.2
50 to 60	39	28.0
60 to 70	8	5.1
Over 70	3	2.1

Sex. In this series there were 103 males (73.6 per cent) and 37 females (22.4 per cent.), or approximately 3 males to each female. Table II shows the number of each sex at different decades; 57 per cent. of the ulcers in women were between the ages of forty and sixty. In these two decades occurred 47+ per cent. of the ulcers in males. No case occurred in females after the sixth decade.

TABLE II.

Years.	Males.	Females.	Total.
0 to 10			
10 to 20			
20 to 30	14	7	21
30 to 40	29	9	38
40 to 50	25	6	31
50 to 60	24	15	39
60 to 70	8	0	8
Over 70	3	0	3

Nationality. American-born furnished 98 cases. The remainder were largely Swedish, Irish, and Canadian.

Occupation. A widely diversified range of occupation was exhibited. In the list were 46 farmers (32 per cent.), 5 physicians, 2 stonecutters, 2 blacksmiths, 2 miners, 1 brickmaker.

Habits. The histories indicate that ulcers occurred in 46 (32 per cent.) individuals using alcohol. In 10 there were evidences of its excessive use; 5 of the cases were heavy smokers.

Dietetic Errors. No definite data with respect to this feature is available. The occupational statistics may be suggestive.

Previous Infectious Diseases. A history of typhoid fever was obtained in 26 (18.9 per cent.). Pneumonia was noted in 6, scarlet fever in 8, measles in 8, syphilis in 5, gonorrhea in 6, la grippe (severe) in 4, rheumatism in 3, diphtheria in 2, smallpox in 2, malaria in 8.

In 2 cases there was nephritis; in 1 cirrhosis of the liver.

12 (8.5 per cent.) had previously been operated upon for appendicitis, and 2 for gallstones. These figures are instructive taken into consideration with the extragastric operative findings (*vide infra*).

Anemia. Where specifically noted the hemoglobin averaged 72 per cent. (Dare).

Nutrition. In 97 of the 140 cases definite figures were available respecting weight loss. The average loss was 20.5 pounds; the minimum loss was 5 pounds, the maximum 65 pounds. The rate of loss varied. In some cases patients were not aware of loss until weighed in the examining room. Other patients had lost weight rapidily, for example, 65 pounds in six months, 30 pounds in six weeks, 25 pounds in six weeks, 20 pounds in five weeks, 25 pounds in three weeks, etc. Even rapid weight loss was rarely associated with cachexia usually evident in malignant disease. Night pain with loss of sleep, constant pain with fear of aggravation on eating, or caution in diet on account of recent hemorrhage were prominent factors associated with rapid weight loss.

12 cases showed progressive gain in weight; 21 had neither lost nor gained.

Appetite. In 52 the appetite was noted "poor," in 52 "fair," in 36 "good." Frequently the appetite is lost in acute attacks of pain or distress. The dread of bringing on distress by food

ingestion sometimes causes a poor appetite habit. The same may be said of persistent "dieting."

Bowels. In 26 the bowel movements were "regular," in 12 "sluggish," in 92 (65+ per cent.) "constipated." In 10 there was diarrhea.

Character of Complaint. 104 (74.2 per cent.) gave histories of discomfort intermittently ("attacks," "spells," etc.). In 36 (26.6 per cent.) instances the ailment was continuous. In many cases there was an early history of "attacks," with recent change to continuous discomfort, frequently associated with weight and strength loss. The "attacks" were variously stated as three to five years, two to three years, or two to six months or two to five weeks apart. They were often noted as lasting a few hours or days to two to six months, irrespective of medical or other treatment. The attacks frequently bore relation to the seasons—spring and fall being favorites.

Previous Disorders of "Digestion." 81 per cent. of the cases came with a diagnosis, frequently self-given, of "dyspepsia" or "indigestion," usually "chronic." Table III furnishes significant and etiologic information (not altogether useless diagnostically) respecting this class of cases.

TABLE III.—Duration of Symptoms.

Years.	No. of cases.	Per cent.
Less than 1	8	5.7
1 to 5	30	21.4
5 to 10	32	22.8
10 to 15	29	20.7
15 to 20	14	10.0
20 to 25	9	6.4
25 to 30	7	5.0
Over 30	11	7.8

The table makes apparent that nearly 54 per cent. of the patients had been affected with disorders of "digestion" for from five to twenty years before operation; about 21 per cent. had been ill less than five years.

Age has only relative importance in the estimation of duration of an ulcerative process in the stomach. Frequently patients in the sixth decade of life have been perfectly well to within a few months of the disability that finally leads to operation (for example, six months, age fifty-eight years; five months, age fifty-three years; three months, age fifty-three years, etc.), while young adults give a history of from ten to twenty years of "indigestion."

SYMPTOMATOLOGY. 1. PAIN. Of the 140 proved ulcers without food retention in the series, pain is the one constant complaint.

(a) *Character of Abdominal Discomfort.* This was styled "distress" in 17, "burning feeling" in 21, "gnawing" in 25, "dull ache" in 33, severe ache in 13. In 31 there was history of colicky attacks ("cramps," "doubling up," tearing," etc.). In 18 instances (12.7 per cent.) these were severe enough to require hypodermic admin-

istrations of opiates. In 64 instances (45.7 per cent.) there were sensations of "upward pressure." In 17 (12.2 per cent.) pain or distress was continuous or appeared irregularly. In 27 instances (19.2 per cent.) night pain was a distressing feature.

(b) *Location, Symptomaticly, of Abdominal Discomfort.* In 112 cases (80 per cent.) discomfort was said to be epigastric; in 29 epigastric to the rib edges (more often to the right); in 18 in the "pit of the stomach;" in 8 in the abdomen generally; in 2 in the "small of the back."

(c) *Transmission of Pain.* In 52 instances (37.1 per cent.) no transmission was given. In 25 cases pain was referred to the back (right side 22, left 3), usually below the tip of the scapula; in 25 cases to the rib edges (right 20, left 5); in 10 to the lower esophagus; in 7 to the infranavel region; in 7 to the shoulder-blades (right 5, left 2); in 3 each to navel, nipples, thorax generally, and "tip" of the sternum; in 2 to the throat.

(d) *Food Relation.* In 123 cases (87.8 per cent.) pain has a definite relation to ingestion of food. The summary in Table IV demonstrates the actual time relation of food and abdominal discomfort.

TABLE IV.

Time of pain in hours after eating.	No. of cases.	Per cent.
Immediately	4	2.8
Less than 1 hour	17	12.2
1 to 2 hours	22	15.7
2 to 3 hours	33	23.7
3 to 4 hours	34	24.7
4 to 5 hours	10	7.1
Over 5 hours and irregularly	20	14.0

Some overlapping is exhibited in Table IV, inasmuch as pain may vary as to time in the different attacks. It will be noted that in more than 79 per cent. of instances, pain appeared within four hours following the ingestion of food. The taking of food frequently temporarily relieved actual pain, as shown below.

(e) *Relation of Time to Pain or Distress to Location of Ulcer.*

TABLE V.

Location of ulcers.	Less than one hour, p. c.	One to two hours, p. c.	Two to three hours, p. c.	Three to four hours, p. c.	Four to five hours, p. c.	Over five hours, p. c.	Irregularly.	Total.	Per cent.	Night pain.
Pyloric	6	5	23	19	6	0	6	65	46.4	12
Prepyloric	0	1	1	2	1	0	0	5	3.5	0
Lesser curvature	5	10	13	7	3	1	4	43	30.7	14
Near cardia	4	2	1	2	0	0	0	9	6.4	0
Posterior wall	4	2	2	2	1	0	1	12	8.5	1
Anterior wall	0	0	1	1	0	0	0	2	1.4	0
Total	19	20	41	33	11	1	11	136		27

Unclassified, 4. Night pain cases not included in totals.

Table V demonstrates that irrespective of the location of the ulcer, 83 per cent. have pain or distress within four hours after eating, and more than 54 per cent. have pain or distress within two to four hours after eating. More than 64 per cent. of ulcers involving the pylorus have pain from two to four hours after eating; more than 53 per cent. of lesser curve ulcers have pain from one to three hours after eating; more than 66 per cent. of ulcers near the cardia have pain less than two hours after eating, more than 44 per cent. less than one hour after eating; more than 66 per cent. of ulcers on the posterior wall have pain within three hours after eating, and 33 per cent. have pain within one hour after eating.

(f) *Pain Control.* Except in acute attacks (for example "colics," perforation, etc.) gastric ulcer pain is usually eased or relieved by limitation of the amount and character of ingested food (diet), the taking of food when distress is marked (food-ease), the neutralization of acid by the alkalies, or by emptying the stomach (vomiting or lavage). As has been shown in this series, opiates were required in 12.7 per cent. of instances, usually in aggravated "spells."

Table VI demonstrates the relative value in our series of the various common pain controls. The tabulations may be so read as to show the relative frequency of relief from any combination of pain controls. The most common combination of controls proved to be diet, food ingestion, alkali, and vomiting.

TABLE VI.—Pain Control.

Type of control.	Total cases.	Food.	Vomiting.	Liquids.	Alkali.	Lavage.	Diet.	Rest.	Pressure.	Opiate.
Food	93	0	49	14	68	14	83	15	5	11
Vomiting	71	49	0	9	41	11	65	10	2	7
Liquids	16	14	9	0	13	4	14	1	2	0
Alkali	82	68	41	13	0	9	77	9	3	10
Lavage	15	14	11	4	9	0	12	1	0	0
Diet	121	83	10	1	9	1	0	12	1	13
Rest	20	15	10	1	9	1	12	0	1	3
Pressure	7	5	2	2	3	0	4	1	0	1
Opiate	18	11	7	0	10	0	13	3	1	0

Explanation: Read times each control gave distress relief in column "Total Cases." For combinations of pain controls read table up and down.

Table VII attempts to correlate these factors with respect to the locations of the ulcer demonstrated operatively.

(g) *Relation of Position of Ulcer to Pain Control.*

TABLE VII.

	Diet.	Food relief.	Alkali.	Vomit.
Pyloric	57	49	37	36
Prepyloric	0	0	0	0
Lesser curvature	51	37	38	26
Near cardia	3	2	1	2
Posterior wall	7	5	4	3
Anterior wall	4	3	3	1
	132	96	83	68

(h) *Areas of Abdominal Tenderness by Palpation.* Of the 140 proved ulcer cases, 126 (95 per cent.) exhibited epigastric tenderness. In 109 (77.8 per cent.) the tenderness was more marked to the right of the midline. In 17 (12 per cent.) the tenderness was prominent to the left of the midline. In 23 instances (16+ per cent.) there was special tenderness in the "pit" irrespective of general epigastric sensitiveness. In 20 instances (14+ per cent.) there was definite exaggeration of tenderness at the right rib border, distinct from widespread epigastric muscle spasm. Five patients (3+ per cent.) exhibited special left rib margin tenderness. In 5 cases (3+ per cent.) the area just above the navel was painful to pressure. On but 1 patient was no abdominal tenderness demonstrated. Ridges, invariably tender, were palpable four times.

(i) *Relation of Areas of Abdominal Tenderness to Location of Ulcer as Found at Operation.* Table V shows that of the 140 ulcers examined, practically half (49.9 per cent.) were pyloric or prepyloric, while more than four-fifths (80.6 per cent.) of the entire series were located at the pylorus and the pyloric half of the lesser curvature.

It has been shown above that in 95 per cent. of our cases here reported there was definite epigastric tenderness. While 46.4 per cent. of all the ulcers were located at the pylorus, in only 14+ per cent. was there increased tenderness toward the rib margin, that is, the anatomic situation of the pylorus. While 30.7 per cent. of all the ulcers were on the lesser curvature, but 16+ per cent. of the cases showed definite tenderness in the pit or midepigastrium.

We have also shown that symptomaticly the patient's complaints of distress are in close harmony with the physical evidences of tenderness. In this classification 80 per cent. referred the pain to the epigastrium generally, 14 per cent. to the right costal arch region, and 12.8 per cent to the pit. There were 8 (5.7 per cent.) ulcers located at or near the cardia. In more than twice that number there was noted high pit tenderness.

It would seem that only when taken with other observations are pain areas, symptomaticly, or points of abdominal tenderness of value in definitely localizing ulceration of the stomach.

(j) *Relation of Evidences of Perforation of Gastric Ulcer to Actual Evidence of such as Demonstrated at Operation.* In our series, 46 cases (32.8 per cent.) had history and physical findings of acute or chronic perforation. In 24 cases (17+ per cent.) suggestion of perforation was possible. At operation 51 (36.4 per cent.) ulcers had perforated (9 acute, 3 subacute, 39 chronic). It would seem that only when history and physical findings of perforation are quite marked can one safely prognosticate an operative finding with fair degree of certainty.

2. VOMITING. (a) *Frequency.* This proved a prominent symptom. Of the 140 cases considered, 99 (70.7 per cent.) gave a history

of at some time vomiting sour fluid, food, or blood. Of the 99 cases, 65 vomited sour fluid alone, 24 vomited sour fluid and food. In the series 50 cases vomited but had no hematemesis, 31 vomited and also had hematemesis, 18 had hematemesis alone. Ten cases regularly *induced* vomiting of sour fluid and food to gain relief from pain.

Of the 99 vomiters, 39 vomited regularly. Eleven had "spells" of vomiting with vomit-free intervals of greater or less length, while 49 vomited only occasionally.

Nausea, Waterbrash, Eructations: In 12 cases, nausea without vomiting was a distressing symptom. "Waterbrash" with or without vomiting was prominent in 26 instances (19+ per cent.)

Pyrosis and eructations were noted in 123 (87.8 per cent.).

(b) *Time of Vomiting.* Of the 99 vomiters, in 35 (35.3 per cent.) the vomiting occurred when abdominal distress was most marked. In 28 instances (28 per cent.), ingestion of food precipitated vomiting. In 29 (29+ per cent.) vomiting was irregular. In 7 (5 per cent.) night vomiting was prominent.

(c) *Vomiting Relation to Food.* Table VIII summarizes this class of cases. It will be noted therein that more than 53 per cent. of these cases vomited within three hours following the taking of food.

TABLE VIII.—Relation to Food.

Time.	Number.
Less than 1 hour after eating	6
1 to 2 hours after eating	4
2 to 3 hours after eating	5
3 to 4 hours after eating	6
4 to 5 hours after eating	3
Over 5 hours after eating	4

(d) *Relation of Ulcer Position to Vomiting.* In Table IX we have summarized our experience in this respect with regard to the character of the vomitus and ulcer location. The most marked feature of the table is the numerical evidence supporting the clinical experience that ulcers at the pylorus and pyloric half of the lesser curvature are commonly associated with vomiting. This appears so especially when we recall that this series deals with gastric ulcer where the stomach emptying power has not been interfered with.

TABLE IX.—Relation of Vomiting to Location of Ulcer Found at Operation.

Location.	Blood alone.	Sour fluid and food without hematemesis.	Hematemesis, sour fluid and food.	Food.
Pylorie	10	23	17	9
Prepylorie	0	0	1	1
Lesser curvature	8	21	8	11
Near cardia	0	2	2	0
Posterior wall	0	3	2	2
Anterior wall	0	1	1	1
Totals	18	50	31	24

3. HEMORRHAGE. (a) *Frequency.* While clinically this sign has special emphasis placed upon it, of the 140 proved gastric ulcers analyzed herewith but 57 (40.7 per cent.) gave a history of bleeding. Of this number 47 (33.7 per cent.) had hematemesis, with or without melena; 25 had hematemesis alone; 32 (22.8 per cent.) had melena with or without hematemesis; 10 (7.1 per cent.) had melena alone; 22 (15+ per cent.) had both hematemesis and melena.

Number: The minimum number of hemorrhages was 1. The maximum 10.

(b) *Severity of Hemorrhage.* In 13 instances the patient experienced no particular inconvenience; in 21 there was faintness, while 23 patients actually fainted.

Amount of Blood Lost: This was given as varying from a "half-pint" to "a gallon."

(c) *Character of Hematemesis.* In 2 instances large clots were vomited. In the remaining cases the blood was fluid.

(d) *Relation of Ulcer Location to Hemorrhage.* Our experience is represented in Table X. It may be observed that irrespective of location of the ulcer, hematemesis alone is most common. It is also interesting to observe that melena may accompany an ulcer located anywhere in the wall of the stomach, and that this may occur without hematemesis in a considerable proportion of cases.

TABLE X.—Relation of Position of Ulcer to Hemorrhage.

Location.	Hematemesis alone.	Hematemesis and melena.	Melena alone.	Total hemorrhage each location.
Pyloric	10	12	4	26
Prepyloric	1	2	0	3
Lesser curvature	9	4	4	17
Near cardia	2	3	0	5
Posterior wall	3	1	1	5
Anterior wall	0	0	1	1
Totals	25	22	10	57

(e) *Relation of Hemorrhage to the Character of Ulcer Operatively Demonstrated.* Table XI details our findings. It is apparent that while all classes of ulcer bleed, yet nearly two-thirds (63+ per cent.) of those doing so show some grade of perforation at the laparotomy.

TABLE XI.—Relation of Hemorrhage to Character of Ulcer Found at Operation.

Character of ulcer.	No. of Cases.
Indurated ("calloused") ulcer	16
Acute perforating	6
Chronic perforating	8
Chronic indurated perforating ulcer with adhesions	17
Saddle ulcer	5
Saddle ulcer with adhesions	5
Total	57

4. TEST-MEAL FINDINGS. In the Mayo Clinic series (before mentioned) of operated gastric ulcers (404 cases), it will be recalled that 264 (65.3 per cent.) showed definite food retention by the tests of Strauss and Hansmann. In the remaining 140 cases, which comprise this analysis, 131 (93.7 per cent.) routine test-meal reports are available for tabulation. In 9 instances test-meals were not given, or if given only absence of food retention is noted.

(a) *Blood.* This was noted in 16 (12.2 per cent.) macroscopically or chemically by guaiac or benzidin tests.

(b) *Bile.* Twelve (9.2 per cent.) gastric extracts showed bile macroscopically or by chemical test (Goodel).

(c) *Lactic Acid* was demonstrated 4 times (3.1 per cent.) by the modified Uffelmann test.

(d) *Quantitative Estimation of Inorganic Acid.* The figures quoted are those obtained from filtered gastric extracts obtained about one hour following the Ewald breakfast, which had been preceded twelve hours by a full meal, including boiled rice and raisins.

Inasmuch as pyloric obstruction with food retention masks the true secretory picture in gastric ulcer, the tables compiled from our cases would appear to be especially suggestive.

Table XII details the quantitative estimation of total acidity and free hydrochloric acid by the Töpfer method.

Table XIII summarizes the amounts of "combined" hydrochloric acid.

TABLE XII.—Test-meal Acidities.

	0	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100
Total acidity	0	4	2	5	16	24	29	25	13	4	5	4
Free HCl	5	2	5	23	26	27	18	12	6	5	0	2
Totals	5	6	7	28	42	51	47	37	19	9	5	6

TABLE XIII.—Combined HCl.

	0	0–10	10–20	20–30	30–40	40–50
Combined HCl	4	26	83	17	1	0

Total Acidity: In 79.1 per cent of the cases this ranged between 35 and 75 with an average of 55.

Free HCl: More than 79 per cent. of meals showed free HCl of from 25 to 55, with an average of 42.5, irrespective of ulcer location (*Vide infra*).

"Combined" HCl: In more than 82 per cent. of instances this varied between 10 and 20. Only four times was "combined" HCl absent.

(e) *Relation of Total Acidity and Free HCl to Location of Ulcer Demonstrated Operatively.* The summary to Table XIV demonstrates that total acidity is quite noticeably higher in ulcers involv-

ing the lesser curvature than in those of any other location except on the anterior wall. The 2 cases tabulated in the latter position showed average total acidity of 70. It would seem that this number is too small on which to base conclusions.

TABLE XIV.—Relations of Total Acidity to Location of Ulcer Found at Operation.

Location	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total
Pyloric	0	1	0	9	11	11	15	8	4	3	1	63
Prepyloric	1	0	1	1	1	1	0	0	0	0	0	5
Lesser curvature	2	1	3	4	4	5	10	8	2	0	3	42
Near cardia	0	0	1	0	2	3	2	0	0	0	0	8
Posterior wall	1	0	0	0	4	4	2	0	0	0	0	11
Anterior wall	0	0	0	0	0	1	0	0	1	0	0	2
Totals	4	2	5	14	22	25	29	16	7	3	4	131

SUMMARY.

Average total acidity—pyloric ulcer	56.0
Average total acidity—lesser curvature ulcer	62.4
Average total acidity—ulcer at or near cardia	51.0
Average total acidity—ulcer posterior wall	48.7
Average total acidity—ulcer anterior wall	70.0

Table XV makes apparent that our material showed noticeably greater free HCl in ulcers at the pylorus than in any other class, except the two tabulated as being on the anterior wall. It will be noted that this is the reverse of the figures returned by a consideration of the total acidity above.

TABLE XV.—Relation of Free HCl to Location of Ulcer Found at Operation.

Location	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total
Pyloric	2	2	7	10	13	11	6	5	5	0	2	63
Prepyloric	1	2	0	0	1	0	1	0	0	0	0	5
Lesser curvature	3	1	9	7	12	7	2	1	0	0	0	42
Near cardia	0	0	2	4	2	0	0	0	0	0	0	8
Posterior wall	1	0	3	3	2	0	2	0	0	0	0	11
Anterior wall	0	0	1	0	0	0	1	0	0	0	0	2
Totals	7	5	22	24	30	18	12	6	5	0	2	131

SUMMARY.

Average free HCl—pyloric ulcers	46.5
Average free HCl—lesser curvature ulcers	38.8
Average free HCl—ulcers at or near cardia	35.0
Average free HCl—ulcers on posterior wall	36.8
Average free HCl—ulcers on anterior wall	45.0

Both tables demonstrate that location of ulcer plays a relatively small part as a local "irritative" factor in the production of acidity. The figures returned also show that while high total acidity and free HCl are occasionally met with in gastric ulcer of the class under consideration, they are the exception rather than the rule.

(f) *Combined Hydrochloric Acid.* Table XVI makes evident that in food retention-free gastric extracts combined hydrochloric acid can be almost constantly demonstrated. There is relatively little difference between the amounts where ulcers are variously located. Our series showed a slightly lower average where ulcers were at the cardia than when such were at the pylorus or on either wall of the stomach.

TABLE XVI.—Relation of Combined Acidity to Location of Ulcer Found at Operation.

Location	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total
Pyloric	12	45	5	1	..	..	..	..	..	..	..	63
Prepyloric	1	3	1	0	..	..	..	..	..	..	..	5
Lesser curvature	13	25	4	0	..	..	..	..	..	..	..	42
Near cardia	0	7	1	0	..	..	..	..	..	..	..	8
Posterior wall	3	3	5	0	..	..	..	..	..	..	..	11
Anterior wall	1	0	1	0	..	..	..	..	..	..	..	2
Totals	30	83	17	1	..	..	..	..	..	..	..	131

SUMMARY.

Average combined acidity in ulcer at pylorus	14.2
Average combined acidity in ulcer of lesser curvature	12.8
Average combined acidity in ulcer at or near cardia	12.5
Average combined acidity in ulcer on posterior wall	16.8
Average combined acidity in ulcer on anterior wall	15.0

(g) *Relation of Free HCl Content to Age of Patient.* Table XVII details the result returned by this study. It will be seen while the highest average acidity is shown in the group of ulcers occurring in the third decade, quite comparable averages are returned by analyses in patients in the sixth and the eighth decades. In no decade are the averages very low.

TABLE XVII.—Relation of Acidity to Age of Patient.

Age and number.	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total with meals.
0–10	0	0	0	0	0	0	0	0	0	0	0	0
10–20	0	0	0	0	0	0	0	0	0	0	0	0
20–30	1	0	1	4	6	4	3	0	0	0	2	21
30–40	2	2	8	7	6	4	4	1	2	0	0	36
40–50	4	1	5	6	6	2	1	1	3	0	0	29
50–60	0	2	7	6	7	6	4	4	0	0	0	36
60–70	0	0	2	2	1	1	0	0	0	0	0	6
Over 70	0	0	0	1	1	1	0	0	0	0	0	3
Totals	7	5	23	26	27	18	12	6	5	0	2	131

SUMMARY.

Average free HCl—age 20 to 30	48.2
Average free HCl—age 30 to 40	41.1
Average free HCl—age 40 to 50	39.3
Average free HCl—age 50 to 60	45.0
Average free HCl—age 60 to 70	36.6
Average free HCl—age over 70	45.0
Average free HCl for all ages	42.5+

(h) *Relation of Free HCl Acidity to Pain Time.* The information returned by Table XVIII is suggestive. It is apparent that following food ingestion a progressively increasing number of cases show pain manifestations up to the fourth hour. Between the third and fourth hours, the greatest number complained of distress. The summary of average acidities shows that the degree of acidity increases up to the fourth hour after eating. It would seem that this series furnishes instructive data respecting relation between distress and concentration (?) of free HCl. After the fourth hour there is a progressive diminution in acidity, a correspondingly less number of cases manifest pain in these periods.

Where continuous distress is complained of the average acidity does not appear to be as high as where definite periods of pain following food ingestion are evidenced.

TABLE XVIII.—Relation of Free HCl Acidity to Pain Time.

Time and group.	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total.
1. Immediately, P. C. . .	1	0	0	1	1	1	0	0	0	0	0	4
2. Less than 1 hr., P. C. . .	2	0	2	5	2	1	3	1	0	0	0	16
3. Less than 2 hr., P. C. .	1	1	2	5	5	3	2	0	0	0	0	19
4. 2 to 3 hrs., P.C.	0	0	9	7	3	4	5	2	2	0	0	32
5. 3 to 4 hrs., P.C.	0	2	3	2	12	5	1	1	2	0	2	30
6. 4 to 5 hrs., P.C.	0	0	3	2	2	2	0	1	1	0	0	11
7. Over 5 hrs., P. C. . . .	0	0	2	0	1	0	0	1	0	0	0	4
8. Irregularly .	2	1	2	3	1	0	1	0	0	0	0	10
9. Continuously .	1	1	0	1	0	2	0	0	0	0	0	5
Totals . .	7	5	23	26	27	18	12	6	5	0	2	131

SUMMARY.

Group 1—average free HCl	36.6
Group 2—average free HCl	40.3
Group 3—average free HCl	40.3
Group 4—average free HCl	46.0
Group 5—average free HCl	51.3
Group 6—average free HCl	46.0
Group 7—average free HCl	42.5
Group 8—average free HCl	29.0
Group 9—average free HCl	33.0

Relation of Free HCl to Vomiting: Table XIX shows that more than 60 per cent. of all cases that vomited had free HCl between 20 to 50. The average was 35.1.

Of the non-vomiting class, but 46 per cent. are grouped between acidity 20 to 50. Their average free HCl was 37+.

More than 56 per cent. of the cases giving no history of vomiting had free HCl between 40 to 80. The average in this group was 57.

(i) *Relation of Free HCl to Hemorrhage.* Table XX demonstrates that 57 per cent. of ulcers evidencing *hematemesis* had acidity between 20 to 50. The average acidity was 35+.

More than 57 per cent. of cases giving no history of hemorrhage had acidity between 30 to 60. The average acidity was 46.

Melena. Sixty per cent. of cases had acidity between 20 to 50. The average acidity was 36+.

TABLE XIX.—Relation of Acidity to Vomiting. Free HCl.

Group.	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total.
Vomited . . .	3	4	20	20	20	12	10	3	5	0	2	99
No vomit . . .	3	1	3	6	6	6	2	4	1	0	0	32
Total . .	6	5	23	26	26	18	12	7	6	0	2	131

TABLE XX.—Relation of Acidity to Hemorrhage. Free HCl.

Group.	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total.
Hematemesis . .	2	1	6	14	6	5	5	3	2	0	2	46
No hemorrhage .	5	2	13	11	17	14	6	2	3	0	0	73
Melena . . .	0	1	2	1	3	1	1	1	0	0	0	10
Totals . .	7	4	21	26	26	20	12	6	5	0	2	129

(j) *Relation of Free HCl Acidity to Character of Ulcer.* Reference to Table XXI demonstrates that the highest acidities are associated with perforated ulcers. The highest average acidity is shown to be associated with subacute perforating ulcer.

TABLE XXI.—Relation of Free HCl Acidity to Character of Ulcer.

Group.	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total.
Subacute perforating	0	0	1	0	1	2	2	1	1	0	1	9
Chronic perforating	1	1	1	3	2	4	0	0	0	0	0	12
Chronic perforating with adhesions . . .	0	1	5	9	5	2	3	3	1	0	1	30
Indurated calloused	6	1	11	13	15	8	7	1	4	0	0	66
Saddle . . .	0	1	3	1	2	2	2	1	0	0	0	12
Saddle with adhesions . . .	0	0	1	1	0	0	0	0	0	0	0	2
Totals . .	7	4	22	27	25	18	14	6	6	0	2	131

SUMMARY.

Subacute perforating, average acidity	64.1
Chronic perforating, average acidity	39.1
Chronic perforating with adhesions, average acidity	46.6
Indurated calloused, average acidity	42.1
Saddle, average acidity	43.3
Saddle with adhesions, average acidity	30.0

(k) *Relation of Free HCl Acidity to Nausea.* In 12 instances nausea was a distressing feature. Half of this number had free HCl between 20 to 50. The average acidity of this class was 36.6. The average acidity of the entire group was 49.5.

(l) *Relation of Free HCl Acidity to Pyrosis.* In 22 instances, pyrosis was a prominent symptom. More than 67 per cent. had acidity between 30 to 70. The average of this class was 47+.

TABLE XXII.—Relation of Free HCl Acidity to Nausea.

Group.	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total.
Nausea	1	1	2	1	3	0	1	1	1	0	1	12
No nausea	6	4	21	25	24	18	11	5	4	0	1	128
Totals	7	5	23	26	27	18	12	6	5	0	2	140

TABLE XXIII.—Relation of Free HCl Acidity to Pyrosis.

Group.	0–10	10–20	20–30	30–40	40–50	50–60	60–70	70–80	80–90	90–100	Over 100	Total.
Pyrosis	0	0	2	5	4	3	3	1	2	0	2	22
No pyrosis	7	5	21	21	23	15	9	5	3	0	0	118
Totals	7	5	23	26	27	18	12	6	5	0	2	140

5. OPERATIVE FINDINGS. (a) *Location.* Table V demonstrates the number of ulcers in each situation as found at laparotomy. It will be noted that the pylorus proper was involved in 65 instances (46.4 per cent.), while in 75 cases (53.6 per cent.), the ulcer was in other portions of the wall of the stomach. In 2 instances two ulcers each were found.

(b) *Character of Lesion.* The tabulations already made (Tables XI and XXI show in detail the number of each class of ulcer found on laparotomy. In addition to this general clinical classification, we may state that of the 50 ulcers which were available for microscopic examination, 12 (24 per cent.) were noted as active "inflammatory," 6 (12 per cent.) showed beginning carcinoma. The remaining 32 were indurated or "calloused" ulcers. In 5 cases an existing or suspected lues was an etiologic and prognostic factor.

(c) *Extragastric Lesions Demonstrated upon Laparotomy.* Appendix: In 49 instances (35 per cent.) sufficiently marked evidences of disease were found in the appendix as to warrant its removal. It has already been stated above that 8.5 per cent. of the cases in this series had had appendectomy before coming to the Clinic. The combined figures, 43.5 per cent., indicate that more than two-fifths of all patients of this group had appendix alterations. The observation is sufficiently striking to warrant emphasis from at least three points: (1) The etiologic relation between appendix alterations and coincident or subsequent changes in the stomach wall; (2) the prognostic limitations respecting normal gastro-intestinal function following appendectomy; (3) the advisability

of careful anamnesis and upper abdominal examination of individuals whose only ailment, symptomatically, appears to be located in the right lower quadrant.

Gall-bladder: Operatively, cholecystitis and cholelithiasis were demonstrated in 21 (15 per cent.) individuals. Previous to entering the Clinic, 7.8 per cent. of the patients in this series had already had operations for gallstones or cholecystitis. The combined statistics indicate that 22.8 per cent. had alternations in the gall tract, apart from gastric pathology. Combining the figures from observations upon the appendix and gall-bladder it is seen that nearly two-thirds (66.2 per cent.) of the cases in this report had associated with definitely proved gastric disease, anomalies of these divisions of the digestive mechanism. In addition to the above, Lane kink was found twice, carcinoma of the gall tract once, and pancreatitis four times (2.8 per cent.).

(d) *Operative Procedures.* Table XXIV offers significant information respecting operative versatility required to meet the particular anomaly in the given subject in order to secure maximum results.

TABLE XXIV.

Operation.	Number of cases.
Posterior gastro-enterostomy (Mayo)	49
Gastro-enterostomy + excision	14
Gastro-enterostomy + sutures	24
Excision alone	24
Compression sutures	5
Anterior gastro-enterostomy	4
Pylorectomy or resection without or with gastro-enterostomy	4
Finney	3
Finney + sutures	1
Heinke-Mikulicz without or with gastro-enterostomy	4
Billroth No. 2 + posterior gastro-enterostomy without or with excision	3
Infolding of ulcer	3
Jejunostomy + Witzel	1
Unclassified (plastic)	1
Total	140

In view of Cannon's recent work upon gastric peristalsis, it would appear that choice of operative procedure to fit the case in hand is quite as essential as is the recommending of patients to submit to laparotomy. Table XXIV emphasizes this.

In this series 2 (1.4 per cent.) cases died within a month following operation. One case had chronic perforating ulcer, with adhesions, who developed obstruction, following extensive excision. The other case was one of large perforating posterior wall ulcer, with adhesions involving the pancreas.

The records show that another patient died five months following excision of a perforating anterior wall ulcer, while two years following excision of a posterior wall ulcer a fourth patient succumbed

to general sarcomatosis, primary in the pancreas. To July 1, 1912, no other deaths had been reported.

(e) *Secondary Operations.* Six cases required second operation within one and a half years following the primary laparotomy. The conditions were as summarized in Table XXV. With the exception of the case later developing a duodenal ulcer, the ulcers requiring the second operation were rather unusual either as to character or situation.

TABLE XXV.

Primary operative finding.	Primary operative procedure.	Second operative procedure.
Ulcer of posterior wall and hour-glass stomach	Billroth No. 1 and excision	Posterior gastro-enterostomy for obstruction.
Large calloused ulcer at pylorus	Infolded	Posterior gastro-enterostomy.
Ulcer at pylorus with marked adhesions	Finney	Posterior gastro-enterostomy.
Ulcer at pylorus, with subacute perforation to head of pancreas	Excision	Posterior gastro-enterostomy.
Ulcer at base of anterior wall	Posterior gastro-enterostomy	Duodenal ulcer. Excision, plastic.
High perforating ulcer on lesser curvature	Excision	Posterior gastro-enterostomy.

SUMMARY. The above clinical analysis of 140 cases of operatively demonstrated surgical gastric ulcer without food retention appears to warrant the following statements:

1. In more than one-third of operatively demonstrated gastric ulcers the stomach's emptying power is maintained.

2. 92 per cent. of this group of ulcers occurs between the ages of thirty and sixty. Males are affected three times as frequently as females. The American-born farmer furnishes a large number of gastric ulcers.

3. Irregularity of food ingestion with the use of alcoholic stimulants is not an uncommon concomitant of gastric ulcer.

4. A rather striking frequency of history of previous infectious disease is shown. 18.9 per cent. of our cases had had typhoid fever.

5. A mild grade of secondary anemia is present in the average gastric ulcer.

6. Weight loss averaging more than twenty pounds without marked cachexia was shown in this series. The loss may be so rapid as to frequently suggest malignant disease. Some cases consistently gain weight.

7. Appetite is lost or is capricious in nearly three-fourths of the cases. More than 65 per cent. are constipated.

8. Nearly three-fourths of the cases have "spells" or "attacks" of discomfort, with good health between such. Such a history may extend over thirty years without alarming clinical manifestations. The attacks are usually called "biliousness" or "dyspepsia." They often show a peculiar seasonal relation. In 36 per cent. of

instances the disability is continuous, with or without nutritional disturbances.

9. Abdominal pain or distress is a constant symptom in gastric ulcer. It is "colicky" in nature in more than 22 per cent. of cases, requiring hypodermic medication in 12.7 per cent. It is frequently mistaken for appendix, or gall-bladder disease, and is often associated with such in addition to gastric ulcer. Night pain, with interference with sleep, is present in 19.2 per cent. of cases. 80 per cent. of patients complain of epigastric distress, frequently referred to the right rib margin or the back.

In 87.8 per cent. of proved ulcers, pain, or distress has definite relation to food ingestion. 83 per cent. of cases show pain or distress coming on within four hours following eating. Nearly two-thirds of pyloric ulcer cases have discomfort from two to four hours after eating, more than one-half of lesser curvature ulcers from one to three hours after eating, more than two-thirds of posterior wall ulcers within three hours after eating, and more than two-thirds of ulcers near the cardia less than two hours after eating, while more than 44 per cent. of this class less than one hour after eating.

Discomfort is most frequently controlled by ingestion of food, alkalies, and by vomiting. 12.2 per cent. required morphine.

On palpation, epigastric tenderness is exhibited in 95 per cent. of cases. In more than three-fourths of our series, tenderness was most marked in the right upper abdominal quadrant. 2.8 per cent. of cases showed palpable ridges.

More than four-fifths of the ulcers were located at the pyloric half of the stomach, and this was in general the anatomic area of greatest complaint or distress on examination.

The diagnosis of the character of ulcer to be found on exploration is only possible where a careful anamnesis is made.

10. Vomiting is present in nearly three-fourths of gastric ulcers without food retention. About 17 per cent. vomit food. Only rarely is delayed vomiting observed. Vomiting is induced in more than 10 per cent. of cases to relieve pain. Nearly 40 per cent. of patients vomit regularly. "Waterbrash" is a prominent feature in 19 per cent.; pyrosis and eructation in 87.8 per cent. In nearly one-third of the cases, vomiting comes at the time of maximum abdominal distress. In 28 per cent. the ingestion of food precipitates vomiting; more than 53 per cent. vomit within three hours after eating. In 7 per cent. night vomiting is a feature. Ulcers at the pyloric half of the stomach are most commonly associated with vomiting even when there is no interference with the emptying power of the stomach.

11. *Hemorrhage.* Of 140 proved ulcers in this group, bleeding (hematemesis or melena) was noted in but 40.7 per cent. About

one-fourth of the cases had hematemesis alone, one-third hematemesis with or without melena, while 7.1 per cent. had melena alone.

Severe hemorrhage or frequently repeated moderate hemorrhages are usually associated with faint feelings or actual fainting (40 per cent.).

Hematemesis is more frequent than melena, but melena alone may occur entirely independent of the location of the ulcer. While bleeding is associated with any type of ulcer, nearly two-thirds of those doing so show operative evidences of perforation.

12. *Test-meal Findings.* Acidity: Irrespective of location of the ulcers the average total acidity was 55; the average free HCl, 42.5; the "combined" HCl in 82 per cent. of cases between 10 and 20. Total acidity is most commonly higher in ulcers involving the lesser curvature and anterior wall than where other parts of the stomach are affected. High free HCl is noticeably more frequent where the ulcer is at the pylorus. While high free HCl is usual in cases in the third decade of life, this is not the rule.

Following food ingestion the great majority of cases show pain within four hours. This series shows that during this period free HCl is progressively increasing. Patients complaining of continuous distress do not necessarily have high acidity.

Vomiting is not usually associated with high free HCl. More than half of the non-vomiting cases had higher acidity than was the average of those vomiting. The average free HCl of patients bleeding was 35+. More than half of the cases giving no history of hemorrhage had average free HCl of 46.

The highest free HCl averages are associated with subacute perforating ulcer.

13. *Operative Findings.* More than two-fifths of the ulcers were at the pylorus.

Of 50 ulcers microscopically examined in this series 24 per cent. showed active inflammatory change, 12 per cent. early carcinoma.

In 35 per cent. of cases, diseased appendix was associated with gastric ulcer. In 15 per cent. cholecystitis and cholelithiasis were demonstrated as concomitant processes. In nearly two-thirds of thi group of gastric ulcers, diseased appendix and gall-bladder were revealed operatively. In view of these figures it is evident that all laparotomies should be thoroughly exploratory even when a well-marked gastric ulcer has been demonstrated.

Operative procedure should be adapted to the individual finding on exploration. A routine technique is frequently accountable for poor post-operative progress.

Prompt relief of symptoms with a comfortable after course is the rule following operative treatment of retention-free ulcer cases.

This series shows an operative mortality of 1.4 per cent. Rather more than 4 per cent. required a second operation. This usually occurred in uncommon cases.

THE ECONOMIC ASPECTS OF HOOKWORM DISEASE IN PORTO RICO.[1]

By Bailey K. Ashford, M.D., Sc.D.,
MAJOR, MEDICAL CORPS, U. S. A.

The island of Porto Rico, with its 3606 square miles of territory and 1,120,000 inhabitants, is almost exclusively devoted to the culture of sugar, tobacco, coffee, and fruit, named in the order of their importance in 1912; sugar in the coast lands, tobacco in the foothills and some mountain valleys, and coffee in the mountainous regions. As fully three-quarters of all labor performed on the island is agricultural, and the output of each plantation depends largely upon the laboring capacity of those engaged in tilling the soil, given the fact that all vegetation is luxuriant and no serious natural conditions hinder the raising of large crops, a study of the great scourge of the laboring classes, uncinariasis, will throw a flood of light upon heretofore obscure factors in the economic development of Porto Rico during the last fifteen years, perhaps through centuries preceding this period.

The value of the coffee crop in 1897, American gold, was $7,492,453; that of sugar, $2,456,898; and that of tobacco, $732,117. Coffee formed 70 per cent. of the value of all the exports in 1895 to 1897 and 41 per cent. of all cultivated land was devoted to its production.

In 1910 the value of sugar exported was $23,545,922 (representing over 60 per cent. of all products leaving the island); coffee, $5,669,602; and tobacco, $5,664,128.

The total value of articles purchased from and exported to the United States in 1901 was $17,502,103, and in the fiscal year 1910, $68,595,326, a gain within ten years of 400 per cent.

Thus we see sugar today the life-giving product of Porto Rico with an increase of seventeen-fold its value in 1897; tobacco a promising industry, which is seven and one-half times as important as formerly, and coffee a decadent industry, which has but 75 per cent. of the value it possessed in the days of Spain.

Our study cannot embrace a detailed consideration of the economic problem, but let it suffice to say:

1. That sugar rose in value when it came under the protective tariff of the United States. Coffee fell when Spain's preferential tariff was removed, and, although the bean was of a superior class, it was unknown and unappreciated in the only free market open to it, the United States, where it had to compete with cheap grades.

[1] Read before the Fifteenth International Congress of Hygiene and Demography, Section 4, Industrial Diseases, held in Washington, September 23 to 28, 1912.

2. That the output of sugar was enormously increased by improved methods of culture and by great mills, now among the largest of their kind in the world. Coffee culture has progressed very little, if any, in improved methods: (1) because, from the nature of the industry, machinery plays an unimportant part in its preparation for the market; (2) because the coffee planters were so poor they were unable to keep their estates at anywhere near their full productive capacity, the bushes needing constant manual attention to increase their output. The value of the crop often barely sufficed to pay the interest on their mortgages, and was totally insufficient to meet the expense of improvements tending to increase their production, especially as loans could only with great difficulty be floated.

3. Sugar rose to the surface in an increasing era of prosperity, unhampered by any convulsion of nature, and favored by the benign influences above cited. Coffee planters were surprised by the war in the midst of speculation and borrowing. Their estates, and even their ripening crop, heavily mortgaged, were visited one year after the American occupation by a disastrous hurricane, which dashed to the ground in a day the coffee bushes, and, worst of all, the shade trees, which are necessary for the superior quality of the bean, thus precluding resuscitation of former crop values for at least five years. Many other factors which tended to depreciate the industry might be mentioned, but a fourth element of highest importance remains to be noted:

4. Sugar lands, and, to a less extent those of tobacco, bereft of shade and bathed by a hot sun, are notoriously poorer culture grounds for Necator Americanus than those of coffee. They are far drier, are well ploughed, and well drained. Coffee groves, well shaded, always sopping and generally undrained, and, above all, far more densely worked, are among the most perfect culture grounds for this parasite in the world. Moreover, the laborers in sugar estates were chiefly negroes, who are relatively immune to uncinariasis. They were and still are better paid, better housed, and better clothed than the poor white coffee laborer, with a constitution weakened by chilling, damp winds, insufficient clothing, insufficient and improper food, and general poverty and wretchedness.

The result has been that the lands previously cultivated in tobacco and coffee have been encroached upon by sugar wherever possible, and that tobacco, increasing in importance, has seized upon coffee lands which are materially diminished in area and driven clear to the mountain fastnesses, where they are generally isolated by lack of roads over which to bring their products to the coast.

We are now in a position to understand why the coffee crop in 1901 was valued at but $1,678,765. In 1904, in part due to partial

recuperation of the coffee groves after the hurricane and in part to better prices, it was valued at $3,903,257. From 1904 on the area of land under cultivation for coffee has steadily diminished, and yet the crop has as steadily increased, until in 1910 it was valued at $5,669,902. This means practically but one thing—increase in production. It has not been great, but it is perceptible.

Those who are conversant with affairs in Porto Rico will realize the precarious condition of her commercial future when one reflects that upon one product—sugar, and the market price of that product—depends her prosperity. Sugar is today, relatively speaking, where coffee was in 1897. Let the duty fall from sugar, and tobacco, as yet a weak industry, and coffee, a struggling one, must together support the island. Sugar this day is the mainstay of Porto Rico, but it is far from being the workingman's ideal crop. Only rich men and powerful corporations can grind sugar. Only the large ones financially can supply these mills with sufficient cane to make them pay. Coffee is the country gentleman's crop, the poor man's crop, the Porto Rican's crop. Even when coffee brought but $7,500,000 a year to Porto Rico, the "jibaro," or poor white coffee laborer, was "better off." His dollar "went farther." Coffee holdings are small holdings, and they well distribute wealth here. Why was coffee so depressed when every other industry was booming? No one can justly complain of prices which permit good profit, and at present the price of coffee is nearly what it was in 1895–1897, when the industry was flourishing. The answer of coffee planters is concise: "There was no coffee!" What they mean is that the per acre production was utterly inadequate. That this is improving is seen in figures above cited. The improvement is attributed by some to this factor, by others to that, but no one, no matter how prejudiced, fails to realize that healthy, strong, and abundant labor plays a tremendous part in the future of the coffee industry in the island of Porto Rico.

Thus we can establish the inseparable relation of the health of the coffee laborer to the welfare of the industry; thus we, as medical men, can justly lay claim to a share in the awakening of that industry which in its palmy days brought happiness and contentment to the people of Porto Rico, for in 1904 a campaign was instituted against "anemia," or uncinariasis, the chief cause of the invaliding of the Porto Rican laborer, especially of the coffee laborer, which has culminated in the successful treatment of 300,000 persons of this class. No Porto Rican is capable of denying to the forty or fifty physicians whose efforts through six years have accomplished this result a part in the financial betterment of their people after this tremendous campaign.

Dividing the island into the municipalities bordering on the coast and those of the interior we find that of the former, out of a total population of 618,871 persons, 117,989, or 19 per cent.,

were treated for uncinariasis; and that of the interior, 130,989 of a population of 334,372, or 39 per cent., were so treated. A little over 50,000 were migratory, and their residence could not be fixed. The unit of division, politically speaking, is the municipality as is the county in the United States; but topographically, while the twenty-four interior municipalities are in the highlands, chiefly devoted to coffee culture and secondarily to tobacco, a considerable part of the area of a coast municipality is apt to extend well back into the mountains, and, of course, such territory is given over to coffee. So it may be said, without fear of error, that not over one-tenth of those seeking treatment for their anemia were sugar laborers, not over one-fifth tobacco workers, and the rest came from coffee groves.

In the rehabilitation of this coffee industry only one plan is feasible: to increase the per acre production, and to do this workingmen capable of 100 per cent. of labor daily are needed. Until anemia among this class is thoroughly under control this will be impossible.

THE LABORER. He is a tiller of the soil, pure and simple, living by sufferance in a rude hut he built, but whose ground he does not own. With a large family he is powerless to save any of his earnings, and, as Weyl puts it, it would be a crime for him to attempt it. When not a victim of anemia he is usually a well-nourished, well-built man of medium stature, reserved, suspicious of strangers, unschooled but astute, generous, and respectful. Again eliminating anemia, his diseases are few, as are his vices. He is long-suffering, and, above all, hardworking, but his methods of labor are primitive and wasteful. He is totally dependent upon the outcome of the crop he labors to realize, and, not being a landowner, unable to read and write, he looks to the planter he serves for protection and ideas.

In the mountains he is a coffee laborer and a white man. On the coast he is more frequently a negro or a mulatto, notwithstanding the tendency of late years for the white coffee laborer to work in the sugar fields during the inactive season in the coffee plantation. His food is confined practically to native vegetables and fruits, with rice, codfish, coffee, and condiments. His diet lacks animal proteids and fats, and would be considered below par in Europe and North America. Take away his wages and he lives from hand to mouth on native fruits and vegetables, for rice, codfish, and condiments he must buy.

That Spain's protection of coffee merely brought about a value of $7,500,000 in 1897, when in 1911 $5,500,000 was rendered by far less coffee land, without any protection and with the stormy past already recounted, must be considered notable. Something was certainly missing. When we consider that from 1890 to 1899 the percentage of deaths from "anemia" to the total death rate

gradually climbed from 13 to 22½ per cent.; when we take into account the testimony of druggists and physicians practising in those days to the affect that they flourished, due to the generous sums spent to secure medicine and medical attendance by the laborer; when we realize that when 15 per cent. of the total death rate is due to anemia, the hemoglobin of the average laborer is not far from 50 or 60 per cent.; we cannot but see that Spain's best endeavor fell short from her failure to solicit medical coöperation. Could sugar have attained a value of $25,000,000 a year with a laborer whose hemoglobin is but 60 per cent.? We believe not. A sugar planter fights shy of a physical wreck when he is looking for his laborers, for the work is hard and requires strong men.

When we Americans first landed in Porto Rico our attention was attracted by the muddy yellow pallor of the average laborer in the country. The anemia of uncinariasis is really a rare cause of death in Europe and North America. Even severe cases are, apparently, very uncommon. What is justly feared is the diminution in laboring capacity. But in Porto Rico, with about 300 persons to the square mile, with ideal cultural conditions for the larvæ, and with small coffee estates in whose shady groves hundreds of barefooted workers daily congregate, clearing underbrush or picking coffee and continually befouling the soil, each laborer receives an almost daily dose of Necator Americanus, a series of multiple infections that fairly break through the most impervious natural immunity and leave an entire class anemic, with a frightful death rate, impossible to comprehend outside of Porto Rico. When it can be said that 30 per cent. of all deaths occurred from anemia in 1900, and that over 60 per cent. of these deaths occurred in the mountains, that two of every hundred died yearly of uncinariasis, has anyone any doubt about the physical condition of the other ninety-eight who lived and were infected under the same conditions as the two unfortunates who lost their lives?

To be more explicit: The hemoglobin of 577 persons presenting themselves for treatment in the Bayamon dispensary in 1904 averaged 43.09 per cent. This was at the beginning of our campaign, and is an especially valuable note, because Bayamon is a coast town where anemia should have been least prominent, but which nevertheless represented the laboring class of sugar, tobacco, and fruit estates, the industries of that rich municipality at that time.

In the same campaign of 1904–1905, of a total of 5490 treated personally by myself and two associates, 22 per cent. were light or very light cases; 19 per cent. were moderate; 41 per cent. were intense or very intense, and 18 per cent. were unclassified. In the six years' campaign, in which 287,528 persons were treated,

3.99 per cent. were very light cases, 20.39 per cent. light, 44.90 per cent. medium, 25.05 per cent. intense, and 4.68 per cent. very intense. There was 0.96 per cent. unclassified. When we consider that we did not classify these cases by hemoglobin percentage in the majority of instances, there may be some objection raised to any attempt at classification; but when we also note that our dispensary physicians had become familiar with the clinical types throughout their life in Porto Rico, and were keen at placing the cases in the class they belonged, it will be seen that the error, if there was any, was exceedingly slight. This we know from our own experience, where a series of several thousands were subjected to a hemoglobin examination at the beginning of the work. Our classification by hemoglobin percentage was as follows:

Between 60 per cent. and normal, a light or very light case.

Between 30 and 60 per cent., a medium or moderate case.

Below 30 per cent., an intense or a very intense case.

The clinical estimate of the grade of the disease was as follows:

A light case: An individual, previously vigorous and energetic, gradually finds himself losing in strength and inclination to work, with symptoms of dyspepsia and perhaps a faint pallor. To his friends and neighbors he is "run down." To unfriendly eyes he is "lazy and good-for-nothing."

A moderate case: A moderately anemic individual, with minus activity of mind and body. The patient looks and feels definitely sick. There is no longer mere disinclination to work, but partial inability. He is pale, exertion brings on throbbing of arteries and palpitation of the heart; sudden changes of position, sudden dizziness. He is half narcotized, as it were.

An intense case: The patient has arrived at that stage when a fatal termination may occur at any time. Extreme pallor, edematous extremities, dilated heart, etc.

On referring to the 5490 cases of 1904, where the taking of hemoglobin percentages on admission was often practised (upon which percentage the type of the disease was based), and comparing this result with the estimate of the case as established clinically in over 280,000 cases subsequently treated, it will be seen that by the latter method the seriousness of each case was rather apt to be underestimated than overestimated.

In whatever light we choose to view it, we can see how sick a laboring class Porto Rico had. My own experience has led me to consider the hemoglobin percentage a fair estimate of laboring capacity between 20 and 85 per cent., although it is wonderful to see the work attempted by an anemic laborer. Below 20 per cent. he is usually *hors-de-combat*, and above 85 per cent. speculation concerning his laboring capacity as affected by the worm he harbors is too uncertain. This means that the average anemic working-

man in Porto Rico lost at least 50 per cent. in working capacity from "anemia."

This unrecognized disease from earliest colonial days has been responsible for the unjust charge of the full-blooded European that the Porto Rican laborer was lazy and indolent, and only after a tremendous cyclone, which threw the coffee-worker upon his own resources, was the mask snatched from the face of one of the most pitiful situations known to medical history. When urged by the planter, by the insular government, by the American people, to arise and go to work, he laid down to die in large numbers, at last incapable of responding to even dire necessity.

Anemia in Porto Rico, influenced by the special conditions incident to the downfall of coffee and by the thousand and one factors which go to weaken the resistance of a defenceless and poverty stricken people to a chronic exhausting disease, deeply affects the laborer, the landowner, and the territory.

The Effect of Uncinariasis upon the Laborer. 1. To reduce his earning capacity: Many times he is paid for the work he accomplishes in a day. This is eminently true of coffee-picking, where he receives from ten to fifteen cents per almud or conventional box-full. Some planters have two sets of wages: one for a healthy man and another much lower, for an anemic. Incidentally they state that they lose money on the anemic, even with his lower wage, but have not the heart to discharge him and so retain him in the hope that he may be cured and swell the numbers of his no-too-numerous workers.

2. To sap his scanty wage from the purchase of medicines and, in some cases, from doctor's fees: The amount of patent blood restorers sold in Porto Rico in past years is astonishing. When finances here were at their lowest ebb after the cyclone this ghoulish industry saw its best days. Doctors could not possibly reach the sick rural population, even had they desired, for the municipal doctor has on an average 15,000 people to attend, often more. These were practically all indigent, and 70 per cent. were more or less sick. They lived not in town or hamlets, but in every nook and cranny of the municipality, nine-tenths of whose population was distributed throughout the rural districts, unapproachable by roads, and generally reached alone over breakneck trails. Over five visits a day to such sick was impossible, and only the few fortunate ones had a modest fee to tempt a physician's call. The rest had to depend upon the lying promises of patent medicines and charlatans.

3. To clog his mentality and reduce his spirit: "Over all the varied symptoms with which the unfortunate jibaro, infected by uncinaria, is plagued, hangs the pall of a drowsy intellect, of a mind that has received a stunning blow. . . . There is a hypochondriac, melancholy, hopeless expression, which in severe

cases deepens to apparent dense stupidity, with indifference to surroundings and lack of all ambition."[2]

Such people are unable to act on their own initiative, and have to be driven to work and told each thing separately several times before they understand.

4. To prevent him from avoiding infection: The earnings of a family averaged in 1904 according to Weyl, the expert of the Department of Commerce and Labor of the United States, considerably less than $100 a year, and there was work available upon only four days in the week. Nine months in the year the majority had no steady work and during the other three months, or at the time of the coffee harvest, the whole family was employed and payment was made, in coffee plantations at least, according to amounts picked. Fifty per cent. of a normal picking was 50 per cent. lost directly from disease. Should every cent of his earnings be spent for food, his ration would still be inadequate for his working necessities. In this way shoes were an impossible luxury. His miserable physical and mental condition, lack of market from impassable roads, lack of beasts of burden with which to work, made cultivation of garden patches out of the question.

5. To prevent his seeking employment elsewhere than in the coffee grove: Coffee laborers, sick with anemia, are not wanted on sugar plantations where there is less chance of infection and better pay. Thus his infirmity peonizes him and binds him to the grove.

The Effect of Uncinariasis upon the Planter. 1. If the roaming coffee picker could earn but a scant 50 per cent. of what he should earn in health, the regularly employed, living under practically the same conditions, could not be expected to earn more. As a matter of fact, even with the ridiculous wage paid in 1904 (thirty cents), the planter lost money in inefficient labor. In a visit made by me to a coffee plantation about two years ago, so remote from the stations for the treatment of anemia that the laborers were nearly all uncured anemics, I was told by the planter that he was thoroughly discouraged and was about to give up; that he had 1800 acres of the best coffee land, much of which he could not afford to put under cultivation, owing to the miserably insufficient output of the part already cultivated, and that he calculated his loss from sick laborers at about 50 per cent. It was then afternoon and the harvest time; the pickers were returning from the grove and depositing their day's collection in the mill. I stationed myself at the door and asked each one what his picking had amounted to on that day, having first established the normal amount which they should have picked per man. The average of some two hundred laborers was 50 per cent. short, and more, of what it should

[2] Uncinariasis in Porto Rico, Senate Document, No. 808, 1911, Government Printing Office, Washington, D. C.

have been, or two almudes a day. The amount received for a box full, or almud, varies with the abundance of berries, but on that day was twelve and a half cents an almud.

So here were two hundred people who had lost at least $50 from a curable and preventable disease in one day. To have seen those poor rain-bedribbled, muddy, barefooted anemics one wondered how they ever brought in the coffee they picked, and, as a matter of fact, some stated that they had to be helped in by stronger comrades! Of these pickers many were pointed out to me as regularly employed peons of the estate, and these were indistinguishable from the rest, as far as the degree of their anemia went. When the incentive to make as large a picking as possible was only able to produce 50 per cent. of a healthy man's output, can we expect that these peons, working by the day and in the same physical conditions, should yield more for a wage?

2. With all the peons the planter could afford to pay, a large part of his estate remained uncultivated, or, if all cultivated, it would be so poorly worked as to yield only a fraction of its normal output.

3. The ideal of the planter is to secure enough peons to almost handle the crop, leaving a minimum to be employed at harvest time, for such itinerant laborers have to be provided for during two or three months in lodging, often for a meal, etc. The larger the number hired at harvest time the greater the expense aside from the wage. In the presence of an anemic peon class, no planter can make economic calculations on his crop.

4. There is at present a scarcity of labor in the coffee plantations. Many good laborers have left the plantation to seek employment in the sugar and tobacco fields, where the pay is better. But the men who leave are the cured cases of anemia, who otherwise would not be acceptable to the sugar estates. The result is that the planter in the mountains has to pay a higher wage than before, and still struggle with his anemics. This is a class that is rapidly disappearing, but the fact remains that it looks as though the coffee men would have to fight anemia to the bitter end, and long after the scourge will have ceased to become a serious menace to the success of the sugar and tobacco industries.

The Effect of Uncinariasis upon Insular and Municipal Government. 1. In a country where so large a percentage of the inhabitants live from hand to mouth, without any money saved for emergencies, in the presence of a disease which palpably affected 70 per cent. of the rural laborers, and caused in 1900 twelve thousand deaths, the resources of that country are strained to provide for them. About one-half of the insular taxes are covered into the insular treasury for roads, education, etc. Local roads, street construction, and other purely municipal expenditures have to be provided by the municipality. Were this municipality to provide for the proper

treatment of all its indigent sick, including expenditures for medicines, it would irremediably go bankrupt. As a matter of fact the paltry sums appropriated for this purpose never meet the situation. In many municipalities the proposals to furnish medicines for indigents were bid upon by local pharmacists, and in a month or so the entire amount was spent for the fiscal year. Even these sums of money, not always wisely spent and not large, represented, nevertheless, a great effort on the part of the poor town.

2. The property values naturally depend indirectly on the output, and when the properties are only partially developed the assessments fail to yield what they should.

3. The laborers employed by the insular government were apt to be the more anemic ones, the best having been absorbed by the plantations. In fact, these very sick were employed on roads at enormous expense at the time when it was supposed that their condition resulted from starvation, and as a measure of relief to the poor. No one can ever know what percentage of these appropriations was lost from inefficient labor.

When all is said and done, it is plain that to permit the coffee industry to die out in Porto Rico is really unnecessary, and very harmful. It is to many minds the crop of crops for the interior of Porto Rico, and its loss will ultimately spell ruin to sugar and tobacco, for these Antillan Islands, bared of their trees, become subject to long droughts and torrential washouts. This has actually happened, apparently, on the south coast, where a $3,000,000 to $6,000,000 irrigation plant is seeking to save Guayama, Salinas, and Ponce sugar. The mountains to the north are scarred and bare, and, for lack of the roots of bushes and the shade of trees to store up and gradually deliver by hundreds of little streams an ample water supply to the rich coast lands below, one of the richest sugar districts on the island is threatened. All of this aside from other considerations already mentioned.

Uncinariasis affects the whole island, directly and indirectly, but it is the chief bane of the coffee industry. To solve the coffee problem no plan is complete, nor would such a plan be successful, which takes no account of this medicosocial problem. In Weyl's report of labor conditions in Porto Rico in 1904 to the Department of Commerce and Labor of the United States we find the following:

"One of the most important of all the factors influencing the condition of the laboring classes of the island is the disease of anemia. This disease, which mainly attacks the poor of the island, more, perhaps, than any single factor, impairs the industrial efficiency of the great mass of Porto Rican laborers. The economic importance of the disease cannot be overestimated . . . the disease is so widespread as to be considered practically universal. The effect upon the conditions of the laboring classes of Porto Rico of completely obliterating the disease of anemia would be

almost incalculable. Many persons who are now too sick and weak to work would then be enabled to do so, and the industrial efficiency, as it is affected by the muscular strength, the nervous energy, the physical endurance, and the intelligent direction of work of the people would be vastly increased. An energetic movement with a view to the obliteration of the disease is probably the greatest single step which can be taken at the present time toward improving the industrial efficiency of the laboring classes of Porto Rico."

From 1904 to 1910 inclusive there have been treated for their anemia by a special service 300,000 persons in round numbers. This number will be much increased by adding the fruit of unofficial work, as follows:

1. Cases treated by physicians not connected with the service: Today there is hardly a physician who does not treat the anemic jibaro with thymol. Many times this is done without a previous fecal examination, in spite of our protests, but inasmuch as 99 per cent. of such cases are due to uncinariasis, great good results therefrom.

2. Cases treated by religious societies and medical missions: Their number is large, and they contribute in a most practical way to the general work.

3. Cases treated by charlatans: Remembering what has been said concerning the difficulty attached to reaching a doctor from the remote barrios of a municipality, is it any wonder that the more calculating jibaros learn the simple technique of treatment and apply it extensively for a consideration? That this is by no means uncommon is seen by skilful questioning throughout these barrios. A vigorous war upon these interlopers has been carried on from the first, but it is hopeless to expect to catch them all.

4. Cases treated by the family: The administration of thymol and salts for anemia is rapidly becoming a family remedy in certain parts, as quinine and calomel is in our South. Even some proprietors of estates are gingerly taking it up. Of course, this too is all wrong, but what can be more natural? Theoretically it is hard to obtain drugs without a physician's order, but in practice it is by no means difficult.

5. Cases treated by the officials of the anemia service in the intervals between appropriations to continue the work: On several occasions there was a hiatus between the ending of the fiscal year and the reëstablishment of the anemia service. On one occasion the legislature was convoked in special session for the purpose of providing for the irrigation of the south coast and to reappropriate funds to continue the anemia work which it had failed to do at the regular session. In these intervals our physicians kept their stations open and worked without pay, although their records were no longer kept as they had been before. In addition to all

this there have been many thousand cases treated by the present sanitary service, which took over the work on July 1, 1910.

Hookworm disease probably gained its foothold in Porto Rico in 1530, nearly four hundred years ago. In 1788 Fray Iñigo Abbad states that "the jibaros had the color and aspect of convalescents." How many years this color and aspect had been observable he does not say, but we can safely affirm that for two hundred years Porto Rican anemia had been explained by the compound theory of improper food, tropical climate, and malaria.

To change the fixed belief of a people, the heritage of two hundred years, was no easy matter. From 1899, when this anemia was first identified by the writer as ankylostomiasis until 1904, when the real campaign against it began, was a period of hard work in propaganda and scientific study.

The result of the universal application of a specific remedy for this anemia has surpassed our most extravagant hopes. Today a bad case of uncinariasis is rare indeed along the highways of Porto Rico, where before in every town the traveler halted he was besieged by pitiful beggars in the last stages of the disease, unable to work and driven by hunger to implore charity from passersby. Few cases of moderate severity are seen, and, indeed, the color and aspect of the Porto Rican people can no longer be described as that of convalescents.

The mortality from anemia is but one-eighth of what it used to be. The total death rate has fallen from 42 per 1000 in 1899–1900 to about 22 per 1000 in 1912, and only in the mountains, in those far-away barrios unseen by traveler and even by the city-bred Porto Rican, does hookworm still stalk abroad, not indeed as it did before, for with the universal treatment of the disease came the universal education of the people, and today there is scarcely a jibaro who does not know that no one need die of his old enemy, "la anemia."

At the close of each year of work the Commission has made it a feature of the annual report to publish letters which demonstrate the enthusiasm and earnestness of those who worked with us to secure our ends. Until 1907–1908 our data had been secured from our physicians, who were really best fitted to judge of the results we were obtaining; but in the last-named year the municipal officials of thirty-seven towns, in each of which stations had been working throughout the year were called upon to express their opinion of the necessity for continuing the work. The Mayor, voicing the sentiments of the council, and, in some instances, the town council by formal resolution, eloquently appealed for its continuance, citing the improvement in the health of the people, the reduction in mortality, and the saving on the municipal budget for medicines. Many stated that they would gladly bear part of the expense to keep up the work, nine passed resolutions calling

upon the Governor to convoke the legislature in special session to appropriate funds enough to proceed with the campaign, and practically all paid a tribute to the work that amply repaid its physicians for the thousands to whom they had administered.

Thus we have the expressed approbation and support of the physician and of the people through their municipal officials. We have a demonstration, eloquent and persistent, of the jibaro's faith in this new "theory," which brought him daily in throngs over many a weary trail without the slightest compunction to our stations. We have the frank expression of the legislature, which from year to year has liberally supplied the necessary funds for the maintenance of the work to a total of nearly $200,000. We have the earnest interest of all the governors of Porto Rico, beginning with Governor Hunt, in 1904, who together with the Honorable Regis H. Post introduced the first appropriation, to the present executive, Governor George R. Colton, all of whom have year after year urged upon the legislature the absolute necessity for supporting this campaign.

In short, no class nor condition of people in Porto Rico, hardly an individual, doubts the necessity of fighting anemia and of paying large sums of money to do so.

Notwithstanding all this, when I decided to write upon this subject it seemed to me that all of this testimony should receive that of the planter himself, who could perhaps say with even more certainty what these benefits have really amounted to. Accordingly, I addressed a circular letter to about 400 sugar, coffee, tobacco, and fruit growers representing every municipality in the island. Although the time is too limited since they were sent for me to have received answers from all, I give after each of the following questions the composite answer made by the 224 from whom replies have been received:

First question: "What percentage of laborers, who could perform a full day's work did you have on your estate in 1900?" Answer: 40 per cent.

Second question: "What percentage of efficiency for labor have your peons gained since they have been cured of their anemia?" Answer: 61.7 per cent.

Third question: "What percentage of anemic peons exist today on your plantation?" Answer: 17.5 per cent.

Fourth question: "Do you believe that by curing them your own profits would increase, and if so, by what per cent.?" Answer: Yes, by 40 per cent.

More than half spontaneously appended a warm and sincere expression for the results of the campaign; many demanding that it be kept up, and stating that the island legislature in all its history had never voted money that had been better spent.

I believe that the sentiment of the planter is best expressed by

the following letter (in answer to one of my own, enclosing a copy of the paper I am now presenting) from the president of the Coffee Growers' Association of Porto Rico:

"PONCE, P. R., July 15, 1912.

"DR. BAILEY K. ASHFORD, San Juan.

"My dear Sir:

"In answer to your circular of last June and your communication of the 12th instant, I desire to make the following observations:

"I have carefully read your interesting work on the economic aspects of the campaign against the anemia of this island, and I do not find anything to add to it, nor do I believe that I should have to make any correction in it. You have said everything. The results of this campaign should not be viewed solely in the light of the notable reduction in mortality shown by the statistics, so far as they refer to uncinariasis, but in the return to the sociologic normal of the large masses which the disease had rendered useless for work, in the work these masses are now contributing to our overincreasing production, in the number of human beings saved from beggary and the life of parasites, in the corresponding increase in our commerce, and in the general betterment of an important percentage of our people.

"The shortness of time at my disposal deprives me of the pleasure of making a careful investigation concerning this matter in order to be able to respond to your questions with exactness. I am not able therefore to answer these questions with mathematical precision, but I can, indeed, assure you (and this everyone here in Porto Rico knows) that the laboring capacity of our workingmen has notably increased to such a point, indeed, that an infinite number of laborers, completely invalided by their anemia, and for this reason absent from their work in the plantations, are today performing work that cannot be surpassed in any place.

"There are two facts that speak with overwhelming eloquence for the value of the anemia campaign:

"1. That our production of sugar has been raised from 70,000 to 300,000 tons; the production of tobacco has increased surprisingly; and the coffee crops, with variations due to the rainfall, are now almost what they used to be before the cyclone of 1899. Moreover, there has not been any lack of personnel to handle the increased production.

"2. That in spite of the great number of laborers who descend to the coast, attracted by the work of the sugar and tobacco plantations, they are not missed in the mountain districts of the interior where coffee is cultivated and where the scourge of anemia was greatest.

"In short I believe that everyone here admits, as a fact beyond discussion, that the campaign against anemia has powerfully influenced the increase in the laboring capacity of our working people, those who have been treated being today as strong as the strongest. The important proposition now would be that government and planter should work together, each in his sphere of action, not only to prevent the disease from invaliding as before our country people, but to safeguard those who have been already cured against a reinfection, in order that the fecund work which you and your confrères have done may not be rendered sterile.

"With my best regards, I am, yours truly,

(Signed) X. MARIANI."

(Translation from Spanish.)

When we confront this data with our estimate in 1902, that 90 per cent. of the rural population and some less of the towns were infected with Necator Americanus, and that 70 per cent. of these were more or less sick, it will be seen that this estimate was not far from the truth.

We considered that we had to deal with about 800,000 infected at the beginning of our campaign when the population was 950,000; 300,000 were treated in the six years of existence of the special anemia service, four years of which that service consisted of Porto Rican physicians, under the direction of Dr. Pedro Gutierrez. From 100,000 to 200,000 more have received treatment to date, which have not been included in our official statistics, and 300,000 still require it. But of this 300,000, fully 200,000 are really light cases, or simply worm-carriers, leaving only about 100,000 who are palpably sick. The majority of these sick are in the hitherto inaccessible mountain barriors.

It is a natural temptation to figure out the millions saved per year to employer and employed; the value of lives which would have otherwise been lost; the impetus which agricultural life has received by raising the hemoglobin of the laboring poor of Porto Rico, but I will leave that to each one who hears or reads this narrative to estimate for himself.

Enough has been said to bring to the consciousness of everyone that scientific medicine has made a whole people 50 per cent. better physically than they were before, and has played a winning card in bringing about a 400 per cent. increase in Porto Rico's commerce.

URTICARIA TREATED WITH EPINEPHRIN.

By Arthur W. Swann, M.D.,

ASSISTANT VISITING PHYSICIAN TO THE SECOND MEDICAL DIVISION OF THE PRESBYTERIAN HOSPITAL, NEW YORK; INSTRUCTOR IN MEDICINE IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

In six cases of urticaria which I have treated by the subcutaneous administration of epinephrin the injections were followed by a rapid disappearance of the erythema and wheals.[1] In each case a dose corresponding to about eight minims for an adult of one hundred and forty pounds was given hypodermically, and the dose was repeated in ten minutes. Two doses sufficed in every instance to cause the complete fading of the rash. An improvement was usually evident eight minutes after the initial dose, and was most marked between ten and twenty minutes, during which time, especially in the severe cases, the rapidity with which the eruption subsided was very striking. After twenty minutes there usually remained some erythematous blotches, or small, pale wheals, which continued to fade until the skin looked entirely normal. All itching ceased in from five to twenty minutes after the first dose.

In Case V the eruption did not return until three days later, when epinephrin was again given (see Case VI). In Case II it recurred after seven hours. In the three most severe cases (Cases III, IV, and VI), all of which were serum rashes, the wheals began to reappear in from one to two and a half hours after the initial dose of epinephrin, and increased steadily for from one to three hours more, when the eruption was again at its height. I have no record of Case I, and cannot say whether or not the wheals recurred.

Unfortunately I was not able to be with any of the patients when the rash began to reappear, and therefore had no opportunity of repeating the treatment in such cases. There is no doubt that if the exciting cause of the urticaria is still sufficiently active the wheals will recur in an hour or two unless the treatment is continued. It will be interesting to see whether or not the condition can be relieved for longer periods, or even permanently, by repeated and properly regulated doses.

A brief account of each case follows. For blood pressure curves, see chart, page 376.

Case I.—Boy, aged about twelve years, who while a hospital patient incidentally developed moderate urticaria, supposed to be of gastro-intestinal origin. He was given two subcutaneous injections of adrenalin ten minutes apart. The wheals started to fade

[1] The preparation used was the 1 to 1000 adrenalin chloride solution of Parke, Davis & Co.

soon after the first injection, and rapidly disappeared after the second. I have no records of this case, and cannot say whether or not the wheals returned.

Case II.—Man, aged twenty-eight years, who for some time had had two or three attacks every year of swelling and redness of the fingers and toes, generally but not always associated with urticaria. When seen by me he had many small wheals and irregular red blotches on the dorsum of both hands and wrists, and complained of a disagreeable sensation of swollen feet, which on walking were somewhat painful, and made him feel as if his shoes were full of cotton. The systolic blood pressure was 113 mm. He was given eight minims of adrenalin solution subcutaneously, and the dose was repeated in ten minutes. Eight minutes after the first dose the subjective sensations in his feet were less marked, and the wheals and blotches on both hands and wrists were fading. In twenty minutes only a few faint red blotches on his left hand remained, and one foot felt slightly swollen. In thirty-two minutes no trace of the eruption remained and both feet felt entirely normal. The patient remained well for seven hours, when the condition returned less severely than before.

Case III. (Diphtheria).—Boy, aged three and a half years. Weight about thirty-five pounds. Systolic blood pressure, 75 mm. The patient had received a single dose of antitoxin eight days before. At this time his abdomen and the inner sides of both thighs were covered with large wheals, around which was a fiery red erythema. Wheals and red blotches were scattered irregularly over his face and both arms, and there was some edema of the foreskin. The eruption was a severe one, and the itching was extreme.. Two minims of adrenalin solution were given subcutaneously, and repeated in ten minutes. In six minutes after the first dose there was a slight diminution of the erythema on his abdomen. In eight minutes a change on his abdomen, face, and thighs was perfectly distinct. In twelve minutes the erythema was nearly gone. The wheals then began to disappear with great rapidity, and in nineteen minutes had entirely faded from the face, abdomen, and right arm, a few still remaining on the left hand and thighs. These continued to fade, and in twenty-eight minutes had disappeared from his hand and right thigh, leaving only a few small whitish elevations on the inner side of the left thigh, which failed to entirely disappear. The edema of the foreskin was also gone. The boy was much relieved for the time being, and for the first time that day went to sleep. One hour and ten minutes after the first dose the wheals began to reappear, and three hours later were as bad as ever.

Case IV. (Convalescent Diphtheria).— Boy, aged ten years. Weight about seventy pounds. Systolic blood pressure, 80 mm. 10,000 units of antitoxin had been given eight days before. Again

in this case the urticaria was severe, wheals and erythema being profusely scattered over the face, neck, calves, and arms. There were a few wheals on the abdomen, and the penis was swollen on one side. He was given four minims of adrenalin solution, and after ten minutes, five minims. Nine minutes after the initial dose there was slight fading on his neck, back, and right calf. Though the eruption was still very marked, the boy said there was no longer any itching. In fifteen minutes the eruption was rapidly fading, and in nineteen minutes was almost gone from the face, neck, and back. In twenty-five minutes the wheals were entirely gone, and all that remained of the eruption was a blotchy erythema, which still persisted on the right arm and both calves. These spots continued to fade, and in thirty-five minutes the skin was entirely clear. In two hours and a half after the first dose of adrenalin the wheals were again appearing, and soon after the eruption was as profuse as ever.

Case V. (Diphtheria).—Boy, aged seven years. Weight about sixty pounds. Blood pressure, 80 mm. The patient had received 10,000 units of antitoxin, and had developed the eruption three hours later. When I saw him, one hour after the first appearance of the rash, there were a few single wheals on the left hip, face, shoulder, and pubis. The right cheek was swollen and blotchy. The rash was of a mild type. Four minims of adrenalin solution were given, and the dose repeated in fifteen minutes. In four minutes the wheal on his hip was distinctly blanched. In eight minutes all the wheals had faded somewhat. In sixteen minutes they were nearly gone. In twenty-five minutes they had entirely disappeared. The eruption did not return for three days, when it recurred in severer form, and the patient was again treated with epinephrin as Case VI. It is interesting to note that in this case the blood pressure failed to rise more than 2 mm., and yet the wheals were affected as in the other cases.

Case VI.—Same boy as Case V, three days later. The eruption was much more extensive this time, the wheals covering in a solid mass the inner sides of both thighs, and being scattered over the face, back, and chest. The systolic blood pressure was now 68 mm. He was given four minims of adrenalin solution, and the dose was repeated in ten minutes. Slight fading was noticeable ten minutes after the initial dose. In nineteen minutes the face and back were entirely clear, the chest nearly so, and the thighs much improved. In thirty-five minutes the eruption had entirely vanished, except for a few small whitish elevations on the inner side of the left thigh, resembling those in Case III. These continued to fade, and fifteen minutes later were entirely gone. In two hours after the intitial dose a few large wheals began to reappear on the back, and an hour and a quarter later the eruption was again at its height.

The striking manner in which the erythema and wheals have subsided in these cases is interesting in connection with work recently done on epinephrin by Janeway and Park.[2] Using strips of excised peripheral arteries they confirmed the work of Meyer[3] and others, which showed that contraction occurred when subjected to epinephrin in high dilutions, and they showed further that the degree of contraction depended not only on the

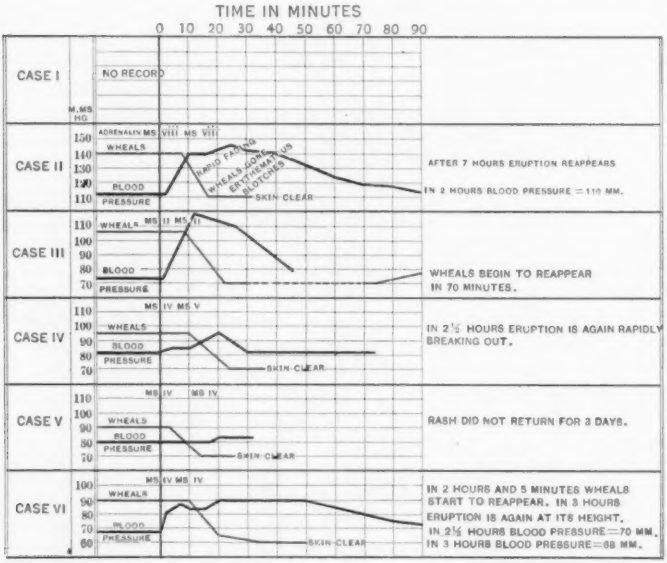

TIME IN MINUTES
0 10 20 30 40 50 60 70 80 90
CASE I
NO RECORD
M.M.S. HG
CASE II
ADRENALIN MS. VIII MS. VIII
WHEALS
RAPID FADING
WHEALS GONE ERYTHEMATOUS BLOTCHES
BLOOD PRESSURE
SKIN CLEAR
AFTER 7 HOURS ERUPTION REAPPEARS
IN 2 HOURS BLOOD PRESSURE = 110 MM.
CASE III
WHEALS MS. II MS. II
BLOOD PRESSURE
WHEALS BEGIN TO REAPPEAR IN 70 MINUTES.
CASE IV
MS. IV MS. V
WHEALS
BLOOD PRESSURE
SKIN CLEAR
IN 2½ HOURS ERUPTION IS AGAIN RAPIDLY BREAKING OUT.
CASE V
MS. IV MS. IV
WHEALS
BLOOD PRESSURE
SKIN CLEAR
RASH DID NOT RETURN FOR 3 DAYS.
CASE VI
MS. IV MS. IV
WHEALS
BLOOD PRESSURE
SKIN CLEAR
IN 2 HOURS AND 5 MINUTES WHEALS START TO REAPPEAR. IN 3 HOURS ERUPTION IS AGAIN AT ITS HEIGHT. IN 2½ HOURS BLOOD PRESSURE=70 MM. IN 3 HOURS BLOOD PRESSURE=68 MM.

CHART.—The subsidence of the rash and its relation to the blood pressure. The heavy line represents the systolic blood pressure. The light line represents the eruption. When declining it indicates fading of the wheals. The point where it reaches the base line marks the time when the wheals have disappeared and only erythematous blotches remain.

strength of epinephrin, but also on the state of tonus in which the vessels were at the time. That is, if the vessels were already somewhat contracted, little further contraction resulted from the epinephrin; whereas, if they were relaxed, the contraction was much greater. Park[4] found that the same principle held good in regard to the dilatation of the coronary artery of the ox, which is produced by epinephrin, and that if the artery were contracted

[2] The Question of Epinephrin in the Circulation and its Relation to Blood Pressure, Jour. Exper. Med., 1912, xvi, 541.

[3] Ueber einige Eigenschaften der Gefässmuskulatur mit besonderer Berücksichtigung der Adrenalinwirkung, Zeitschr. f. Biol., 1906, xlviii, 352.

[4] Observations with Regard to the Action of Epinephrin on the Coronary Artery, Jour. Exper. Med., 1912, xvi, 532.

a much greater dilatation occurred than if it were already in a state of relaxation. He suggested that this might explain the striking relief often produced by epinephrin in cases of bronchial asthma, where the effect on the bronchi is out of all proportion to any apparent effect elsewhere in the body; for as has been observed by Eppinger and Hess,[5] and also by Frank[6] there may result marked relaxation of the bronchi, with little or no rise in blood pressure. In such cases as Park[7] pointed out, the drug seems to have a more or less selective action on certain structures, depending probably upon their state of tonus.

From the results obtained in these six cases of urticaria, it seems probable that in such cases too the vessels in the wheals are in a state of optimal tonus for the action of epinephrin, and that on them the drug has an unusual and selective effect. In contrast to asthma, however, the rise of blood pressure which occurred was in most cases greater than usually follows subcutaneous injections of epinephrin in other types of disease, or in health, and may have been due to a generally relaxed condition of the arterial tree, which one would expect to be present in such cases. A relationship between the rise in pressure and the subsidence of the eruption is shown in the chart, where it is readily seen that in every instance except in Case V the wheals began to fade soon after a marked rise in pressure had occurred, and continued to fade while the pressure was rising or still above normal. On the other hand, the inconstancy of this relationship is shown in Case V, where the rash nearly disappeared before any rise of blood pressure took place, and by the fact that in most of the cases the wheals did not reappear for some time after the pressure had again fallen to its starting point. It is therefore by no means certain whether the disappearance of the rash depends entirely upon the local contraction of the bloodvessels or whether it also depends in part upon some other process. Meltzer and Auer[8] have shown by animal experimentation that epinephrin retards absorption from the tissues into the blood and transudation from the blood into the tissues, and that this effect is maintained well after the blood pressure has fallen to normal. It is possible that this may be instrumental in causing the wheals to disappear, though it would seem more logically to be a factor in preventing their reappearance.

The effect produced in these cases of urticaria suggests that epinephrin might be used to advantage in certain more serious yet similar conditions. One such condition is "angioneurotic edema" in its various forms. At the present time, except for

[5] Zur Pathologie des Vegetativen Nervensystems, Zeitschr. f. klin. Med., 1909, lxvii, 344.

[6] Bestehen Beziehungen zwischen chromaffinem System und der chronischen Hypertonie des Menschen, Deutsch. Arch. f. klin. Med., 1911, ciii, 397.

[7] The Physiologic Action of Epinephrin on the Bronchi, Jour. Exper. Med., 1912, xvi, 558.

[8] The Influence of Suprarenal Extract upon Absorption and Transudation, Philadelphia, 1904, xxvii, p. 8. Reported in Trans. Assoc. Amer. Phys., 1904.

general hygienic management, little can be done for these cases, and it will be interesting to see what can be accomplished with repeated doses of epinephrin. In cases of edema of the epiglottis or larynx due to disturbance of this type epinephrin given intravenously, if its action were similar to what it has been in these cases of urticaria, might well be the means of saving life, when the local application of the drug and other measures had failed.

Another such condition is anaphylaxis, with severe bronchial spasm and edema. From its physiological action on the bronchi and peripheral vessels, epinephrin should theoretically be the most specific of any drug in these cases. That it may relieve the asthma of anaphylaxis, at least temporarily, is well known to clinicians, and its effect on certain urticarias of this type has been shown in this paper. Whether or not it could be made beneficial in every such case if the doses were properly manipulated is a question of some interest. I know of one extreme case of anaphylaxis with dyspnea, but without edema, where epinephrin had no apparent effect, though it is impossible to say what larger and more frequent doses might have done. We know too little, however, of the possible reactions which may in turn follow the primary dilatation produced by the epinephrin to give more than moderate doses in such grave cases, and this point requires further investigation.

The rapidity with which the erythema has faded in my cases suggests the possibility of using epinephrin to differentiate rashes of purely vasomotor origin from those of other types. Hayes[9] suggested its use in diagnosticating serum erythema from the rash of scarlet fever. We have not yet had an opportunity of trying it in a case of scarlet fever, but it is rational to expect that the scarlet rash would fade but little or not at all.

In concluding, I wish to thank Dr. Joseph E. Winters, whose kind permission to work in his wards at the Willard Parker Hospital enabled me to obtain the cases of serum urticaria, and also Dr. R. Hayes for many courtesies extended to me while there.

THE DISSEMINATION AND PREVENTION OF YELLOW FEVER.

By Joseph H. White, M.D.,

SURGEON, UNITED STATES PUBLIC HEALTH SERVICE, NEW ORLEANS, LOUISIANA.

In order to avoid possible misunderstandings, I shall not enter into an argument regarding the relative merits of the observations of Beauperthuy, Knott, and others, but no discussion of

[9] Personal communication.

this subject would be fair unless it embodied the credit which is due to Carlos Finley for arraigning the stegomyia as the cause in the dissemination of yellow fever, and which did not recall the wonderful clinical observations of Carter in the Mississippi outbreak of 1898, in which he noted the apparent discrepancy between the incubative periods of the first secondary case in a house and those following it. This is true, because the notes of these two men were the most important factors in leading the United States Commission under Reed to pursue the proper line of research from the start.

To that commission, Reed, Carroll, Lazear, and Agramonte, we owe the definite, conclusive, and irrefrangible proof that the female Stegomyia calopus is the transmitter of yellow fever from man to man; that she receives her infection during the first three days of the man's illness and does not herself become dynamic for evil short of ten or twelve days, and the further proof that the mosquito is the sole means for such transmission, though naturally we cannot positively say that some other of this genus may not also transmit the disease until all have been tried. It is superfluous to recite the findings of this commission, as they are known to the whole world; but because there has been some inclination shown to still believe in the transmission of the disease by fomites, I think it well to report additional facts coming under my own observation, and bearing on this phase of the matter.

During the 1905 epidemic in New Orleans I arranged that all of our prophylaxis should be based upon the findings of the Reed Commission, and, pursuant to this policy, our yellow fever hospital was screened at every opening so effectively that no mosquitoes could effect an entrance. Only one portal was provided for entrance and exit, which was fitted with triple doors, two strong electric fans blowing outward day and night, and a boy stood in the vestibule to locate and destroy any chance entrant.

All fomites, soiled bedlinen, and clothing stained with vomitus, fecal matter, and blood from over 300 patients suffering from yellow fever, was carried without any disinfection to one of the benevolent institutions of the city, where it was laundered; and this was the only institution in the city which was free from yellow fever during the epidemic of 1905.

Our hospital, containing 120 beds, was manned as to medical staff, nurses, cooks, waiters, scullions, etc., with absolute disregard for the question of immunity, and no member of the personnel became infected, save one young woman, who subsequently confessed she had violated her obligations, and had slept one night outside in what was afterward proved beyond doubt to be an infected house.

Patients were permitted to be seen by friends and relatives, and sometimes whole families were taken into the hospital and

held under observation while one of their number was sick with yellow fever and their house was being fumigated, nor was there reason to suspect that infection was transmitted in this manner.

From the evidence of the commission, and from my own observation in connection with this hospital and with three or four epidemics, it appears to me there is no reason to believe that there is any other means of transmission save through the female stegomyia which has bitten an infected person during the first seventy-two hours of his fever.

The disease presents itself in what has been arbitrarily classified as endemic and epidemic form.

The endemic existence of yellow fever depends upon two factors: (1) The constant presence of mosquitoes of the genus stegomyia, and (2) the presence of a constant supply of non-immune material (people). The latter factor is supplied in two ways: one by population sufficiently large that its birth rate will supply the non-immune material, as is the case in such cities as Habana or Rio Janeiro, and the other by the steady incoming to a smaller town of people from remote places of habitation, such as is the case in communities like Cartagena, where the "paesanos," bringing Tagua nuts, are constantly arriving, resting a few days, and going home. Such cities as Guayaquil and Vera Cruz may supply both conditions.

The Stegomyia calopus is according to my observation entirely a domestic mosquito, and while I would not assert that under such conditions as might annihilate all human habitation near by that it might not breed in natural pools, it is nevertheless true that as matters ordinarily exist it always breeds in artificial water containers, such as cisterns, barrels, tubs, buckets, broken bottles, cans, stagnant drains with brick, stone, or cement sides, etc. It seems instinctively to avoid water courses having weeds and grass around their margin, and in a conversation on this subject with H. W. Thomas, of Manaos, I learned that the one breeding place known to him which was not deemed artificial, fulfilled artificial conditions in that it was a cleft in rock and free from vegetation.

Howard also states that the stegomyia gives evidence in its method of attack of long acquaintance with man, since it always attacks from the rear or under the lower edge of a garment, and never where it can be easily destroyed. He considers it almost as much domesticated as the barnyard fowl. Many have confirmed Howard's findings in this respect, also in regard to its habit of, biting at twilight after it has become accustomed to blood feeding, though prior to that time it is not so discriminating

In 1905 I called the attention of Sir Rubert Boyce to the domestic character of this mosquito, and found him somewhat incredulous regarding my statement that I had never found it in any water containers save artificial ones; but I had the pleasure some months

later of meeting Dr. Boyce on his return from Central America and the West Indies, where he had verified my observations, failing to find the stegomyia in crab-holes and other natural pools.

This is *a propos* in connection with the statement of J. De Goyon[1] regarding French West African work. He states that much attention was paid to crab-holes, that vast numbers of them along the coast offer protection to the mosquitoes, and without noticing the apparent discrepancy, and almost in immediate connection says: "Le Moal has shown that the mosquitoes which inhabit crab-holes were principally Catageiomyia senegalensis and Uranotænia annulata." He then continues: "The larvæ found in odd water receptacles almost exclusively belonged to the genus stegomyia." He calls attention to the danger from non-reported cases, and advises a change in the manner of house construction, gutters, etc. All his observations are excellent, but he fails to note that poorly constructed wooden roofs and gutters furnish excellent breeding places.

K. S. Wise[2] also notes that "Stegomyia fasciata and Culex fatigans were found only in close proximity to human habitations. . . . The larvæ of stegomyia were never present in trenches nor unoccupied ponds." This corresponds with my observations stated at the 1905 meeting of the American Society for the Advancement of Science.

Wise also states that the anophelines breed in trenches overgrown with vegetation, in hollow stumps, etc., and that clearing arrests such breeding; these facts are pertinent to this discussion, because malaria tends to confuse diagnosis, and efforts should be made to eradicate malaria coincidentally with yellow fever.

The question of the flying radius of the stegomyia has given rise to much discussion, and for that reason I would submit some further observations of my own bearing thereon.

During July, August, and September, 1905, the old French quarter of New Orleans known as the Vieux Carré was the most pronouncedly infected section of the city.

The Louisville and Nashville Railroad runs through the river side of this section to its passenger station at the head of Canal Street. I purposely permitted unscreened passenger trains of this line to go out every day, with every seat full of passengers bound through to the North, and these trains were boarded at the Mississippi-Louisiana State line by young guardsmen of the Mississippi State Guard, all of whom were non-immune, who rode in the coaches across the whole State of Mississippi with passengers to the Alabama State line, where Alabama men took up the task of seeing that these passengers did not debark in infected territory.

[1] Revue Scientifique, September 23, 1911.

[2] Annals of Tropical Medicine and Hygiene, December 30, 1911.

I did this because there was no place where these cars would come within less than fifty yards of a dwelling house, and that no stegomyia from an infected room would fly fifty yards in the open sunshine. The result showed that my surmise was well-founded, as there was not a case of any kind of fever among these guardsmen, while there undoubtedly would have been had any infected mosquitoes been in the coaches. Naturally the coaches would have been fumigated had any illness occurred.

Again, on Burgundy Street, a long, low house, the middle one of three just alike, with windows of each exactly opposite those of the others, mostly open, and not more than fifteen to twenty feet between the houses, became infected, and so remained for about thirty-five days before it was discovered that every member of the family had the disease. Neither the neighbors to the right nor to the left visited this house, and neither did any of them contract the fever, though other people who lived at a distance who did visit the house became ill of yellow fever.

I am quoted by Rosenau as saying in 1898 that yellow fever never crossed the street save on a pair of shoes, and I am now even more convinced of the almost unfailing rule that to become infected with yellow fever one must enter a room, with a dim light, where yellow fever has been at least fifteen days before.

It is not to be denied that an infected mosquito might be imprisoned in a bag or piece of furniture and carried to some distant point *nolens volens*, but the contingency is so remote as not to be worth discussion.

It is unfortunate that so much of our work must depend upon deductive reasoning rather than facts, but it is nevertheless true, and for this reason I have submitted so much of this data.

In the sick-room the infected blood-feeding stegomyia finds all the congenial conditions of shade, blood, moisture, rest, and sunshine, and remains there, having practically changed her whole life habit since she tasted human blood; and, so far as my observation goes, she will never leave there unless the sick-room be entirely abandoned and left without even water, as happened in one instance in Baton Rouge, where an obscure case was traced to the fact that the patient slept in an open bay window, within ten feet of an old abandoned shack, where an Italian couple, who had fled from the New Orleans epidemic, camped for a week, during which time the man had a mild attack of yellow fever, and they then fled again, leaving their infected stegomyiæ behind them to infect the woman sleeping in the open bay window eighteen days later. This is the only case known to me where conditions would force the migration of the insect.

The prevention of yellow fever resolves itself naturally into: (1) The prevention of mosquitoes breeding, with the destruction where practicable of existing mosquitoes as a secondary phase; (2)

the isolation of the sick man, together with his infected mosquitoes and the final destruction of these infected mosquitoes.

The former proposition is one of interest in dealing with an endemic centre, and the latter is the one which comes to the fore in dealing with an acute outbreak demanding rapid and effective work.

In attempting to prevent breeding it is advisable to attack mosquitoes and their breeding grounds without regard for genus or species, because in so doing we shall answer the question, "May we not force the stegomyia into new breeding grounds, such as puddles, swamps, etc.," and again by attacking all mosquitoes we eliminate complications in the way of diagnosis, at least in part.

All ground within a quarter of a mile or more of the area to be treated should be reduced to ordinary dryness by drainage ditches and in the end by a system of subsoil drains, so that there will be no surface water to contend with, as ditches may pocket in places here and there and breed mosquitoes.

Thorough policing of the whole area not less frequently than once each week, and preferable once every five days, is essential, and is to be coupled with a clean-up of each water container, such as tin cans, broken bottles, etc., as well as grass and weeds in damp corners of the yard. All regular water containers, such as cisterns, barrels, buckets, tubs, fountains, church fonts, and cemetery urns, must be inspected at short intervals to see that they are not breeding mosquitoes, and to this end screens of eighteen meshes to the inch may be used on all containers, or a constantly renewed covering of refined petroleum may be applied to their surfaces. For the fountain a strong head of water and a number of small fish will suffice. The little minnows, known by the Jamaica negroes as "millions," serve this purpose. For the font, a tablet of bichloride or a small crystal of cupric sulphate, frequently renewed, is suggested, and the same rule will apply to urns, which I have seen swarming with stegomyiæ.

Experience has shown that the people will promise all these things and not do one of them, and that the paid lay inspector will attend to his duties so long as he is under the eye of the sanitarian.

Among the places to be watched as possible breeding grounds are the manholes of the city drainage and sewerage system, also the sagging roof gutter, which is a prolific source of danger, especially where shaded for most of the day. The remedy for the latter is simple: punch a hole in the dependent part with a ten-penny nail, unless it can be torn down entirely. The removal of all roof gutters, allowing the water to fall into paved ground drains and run freely away, is the ideal way to meet this question, and is the method adopted in the Canal Zone

As to the destruction of existent mosquitoes of the genus stego-

myia, it is not impossible, as was proved in New Orleans, but is feasible only because of the habit of the stegomyiæ seeking dwelling with man, and making it therefore possible to destroy them by house fumigation; but such measures meet with objection in houses where there has been no fever, and it is possible that such work is better dispensed with in the interest of popular coöperation, where an endemic focus is being attacked and the work of necessity to be long continued.

In the handling of an epidemic, prompt and efficient work is necessary; this means the immediate isolation of every sick man and his accompanying mosquitoes; nor can this be too carefully done. We are confronted in this connection with the mild case in the negro and negroid, and to the cases on which it is sometimes difficult to obtain a report which we find among the younger members of the poorer class of whites unaccustomed to sending for a physician unless someone of the family is seriously ill. Two factors are predominant in these cases: (1) The ignorance of the class of the medical man usually employed by these people, and (2) the fact that these people, more than any others, object to the attentions of the health officer. It is therefore apparent that too much attention cannot be paid to the ignorant physician, to the slightly ill negro, nor to the young white child in similar case.

In dealing with the houses in which known or suspected cases of yellow fever have been discovered, it was my custom first to see whether the house had been properly screened with eighteen-mesh-to-the-inch wire cloth, and if not, to have screening done promptly, using mosquito netting as a substitute for wire cloth, and having the sick-room itself, as a double precaution, screened from the remainder of the house. The sick-room door can be easily screened by tacking two ample widths of the netting to the top and sides of the door, and attaching a wooden rod to the bottom of each width, so that the ends projecting into the door are higher than those at the side, resulting in the rod dropping into place and pulling the folds together immediately behind anyone passing through. With Guiteras I believe in careful screening, and in covering all cracks around the sick-room; also in the quietness with which this work is done, to prevent disturbing either patient or mosquito. The sick-room window should be screened from a ladder on the outside of the window. In order to prevent escape or entrance through the chimney, a cap should be placed on the top; or failing in this, some loose paper should be burned in the fireplace, with a little petroleum to make a rapid flame, and the front of the fireplace covered with a screen of wire netting.

After the patient is in condition to be removed to another room or house, three days having elapsed since he became ill, he is removed and every crack pasted over into which an insect may hide, and all drawers opened, so that the fumigant used may reach

all places in the room, care being taken that no mosquitoes are shut between the outside screen and the window in closing it. The room and its contents are subjected to either sulphur dioxide or cyanide, burning pyrethrum powder or any other fumigant. The whole house is simultaneously treated in the same fashion if the patient can be removed to another house. Otherwise we must treat part at a time with more than usual care.

I have never deemed it necessary to fumigate detached neighboring houses, but I consider a contiguous and connecting house to all intents and purposes, from a sanitary viewpoint, a part of the infected house, and treat it accordingly.

On August 8, 1905, I undertook, at the request of the Governor of Louisiana and the Mayor of New Orleans, to eliminate an existent epidemic of yellow fever in New Orleans, which had presented to that time 600 known cases, scattered over forty-four square miles of territory, among a population of 335,000, and with many indeterminate foci.

I deemed it necessary, under these conditions, to make an attack on all mosquitoes in addition to killing all infected stegomyia. The result was the total elimination of all yellow fever, nearly all stegomyia, and most of the anophelines and culicidæ by the end of October.

The work was continued for one hundred days from its inception, and the amount expended in round figures was from all sources $325,000, a fraction under one cent per capita per diem.

We expended about $50,000 for hospital equipment and maintenance, and $75,000 for special treatment of infected houses, leaving $200,000 for the total cost of one hundred days of elimination work, such as would be done in an endemic centre, with permanent eradication in view and which includes the overhead charges for all the work, being therefore a more than ample estimate of the cost for this latter class of work. Making allowance for slight inaccuracies in such calculations, the cost of such work would average from six to eight mills per capita per diem—less perhaps in large cities, and more in small towns on account of undue weight of overhead charges in the latter.

The endemic centre has been destroyed at Habana by Gorgas, and later a reëstablishment of endemicity prevented by Juan Guiteras. The same thing has been done at Rio by Cruz, at Panama by Gorgas, and at Vera Cruz by Liceaga; and it cannot be doubted that the consistent application to all endemic centres of the kind of work above described will destroy endemicity in the whole world, and as epidemics are dependent on endemic seed beds for their existence, yellow fever will cease to exist, and Pasteur's postulate that it is possible to eliminate infectious diseases entirely can be demonstrated in this one.

CONCLUSIONS. The mosquito is the only disseminator of yellow fever, and the female stegomyia the only genus and species proved to be the carrier.

Yellow fever is only infective during the first three days of the attack, and the mosquito biting a patient after that time receives no infection.

The stegomyia itself cannot convey the infection to another human until after the lapse of at least ten days subsequent to the ingestion of yellow fever blood.

One attack of yellow fever generally gives immunity—not always.

Feeble susceptibility in the negro is sometimes confused with immunity.

Mild cases are the rule with that race, and this causes many cases to be overlooked.

Destruction of all breeding places for all varieties of mosquitoes, and especially stegomyiæ, anophelines, and culicidæ, is necessary in dealing with endemic foci.

Rapid anti-epidemic work may be confined to destruction of infected stegomyiæ alone; but this is short-sighted.

THE SANATORIUM OF THE FUTURE.

BY HERBERT J. HALL, M.D.,
MARBLEHEAD, MASSACHUSETTS.

THE introduction of more careful diagnosis and the decline of routine treatment, together with the gradual taking up of rational occupations and physical training, in the various sanatoria of the country has been slowly changing these institutions from rest cures in the extreme and objectionable sense to places of real reconstructive opportunity. The fact is that some of the most difficult and important cases of chronic illness cannot be adequately treated in the home, because of conflicting and unfavorable conditions, and because the physician does not have the opportunity to observe the patient or control his life for a sufficient length of time. The hospitals, as they are at present organized, cannot of course meet this requirement, so it seems probable that the sanatoria will become increasingly important as they improve their equipment.

But a great responsibility rests upon these institutions. They can no longer treat all their patients with baths and electricity. I believe they should, first of all, cease to be one-man places. No one man may hope to cope, single-handed, with all the perplexing

questions that the modern sanatorium must face. It seems reasonable that in the future these institutions will be situated near to great medical centres, so that while they give the advantages of country or seashore life they may call frequently into consultation the best men in the profession and in the different specialties. In the European countries the old-established spas may have their corps of physicians, highly trained and experienced in general medicine and in all the specialties. In this country it is too much to ask, at least for many years to come, that each sanatorium should have under its own roof specialists of the highest order; but it is not too much to ask that the best men should be kept in constant touch with such institutions and that their knowledge and experience should be frequently used for the benefit of the patients.

The sanatoria, wherever they are situated, will deal, of course, for the most part with the so-called nervous cases, because such illnesses almost invariably mean long periods of adjustment and reëducation even under favorable conditions. Fortunately modern medicine is coming gradually to a better understanding of the functional nervous illnesses, a better classification and a better treatment and a more serious consideration. The progress of psycho-analysis, for instance, and of the most excellent reëducative methods which are now in vogue bids fair to make clear many an obscure disability and to afford relief where relief might never have come.

Underlying the whole problem of successful management of any chronic illness, and concerning itself intimately with any kind of treatment, psychic, physiologic, or medicinal, is the question of the daily life of the individual—how it shall be lived that any treatment may have its best chances, and how it should be lived that routine and order may, in themselves, be reconstructive and educative.

I have for many years believed that the dependent and artificial life of the sanatoria, as well as the commonly difficult conditions of the home, represented, in the face of nervous or chronic illness, a serious handicap to any kind of treatment. I have believed that we might fatten the emaciated individual, that we might improve the anemia or the feebleness of any case of malnutrition and still leave the patient inadequate and helpless, unless we were able to supply, along with our cure, a training in actual living that would correct the evil effects of the habits of illness and leave the patient ready to meet with the maximum efficiency the requirements of ordinary life.

It would seem that the sanatorium of the future has a special opportunity in the training of the handicapped to meet easily, and so virtually to overcome, their limitations. In this connection I have for the last eight years been studying the possibilities of

the work element in sanatorium life, and I have arrived at certain interesting and suggestive conclusions. I have seen that in a good many cases of psycho-neurotic nature I can obtain satisfactory results by reorganizing the life of the individual by means of graded and progressive occupations. I do not mean by this that I have altogether neglected the ordinary therapeutic agents or that I have failed to consider or to treat such physical illness as may have been involved in my cases of nervous exhaustion, but the principal treatment has been that of adapting the individual to a systematic life of productive occupation, carefully planned to meet and not to exceed his capacity.

I have in many instances purposely neglected going into the subtleties of the individual outlook or into any attempt to correct, by direct advice, the faults of the undesirable habits, and I have seen many and many a mistaken idea, many a disabling excess or extravagance correct themselves, simply by virtue of the regular life and the normal conditions which the work cure, as I have carried it out, imposes. One reason why I have been glad to observe this is because I am, by nature, disinclined to the methods of psycho-analysis, and because I feel that I could not by such means accomplish the results which have been easy in this other way. No doubt many of my colleagues enjoy as little as I do long arguments and the continued study of mental processes. These men will be interested to know that the work cure is often a successful reconstructive measure.

I cannot, of course, say that this treatment, by itself, has been all sufficient in many psycho-neurotic cases, for inevitably other considerations have entered. Moreover, it is impossible to say how much or how little the physical treatment, which has been that of general practice, has availed. I cannot even say that my results are as good or even better than those of the usual sanatorium. Long experience and much classification and analysis alone can justify statements of results in chronic cases of any kind. There is so much chance of error that, in dealing with such indefinite conditions, we may never be able to make dogmatic statements. But if one may rely upon the improved morale of patients, and if we take increased efficiency as our standard of comparison, I believe that I may speak very favorably of the work cure.

In describing the work cure and its possibilities, I wish first of all to disclaim any desire or intention of making it a universal remedy or a cure-all. I have not gone far enough with it yet to know surely to what classes of cases it is best applied, or when it must not be used at all. But the experience of eight years has taught me that the application may be a wide one if we make it merely the background and basis of any physical or psychic treatment which may be indicated. And I believe that continued experi-

ence will make even clearer my conviction that there are many tedious cases of neurasthenia, complicated or not by physical conditions, which will yield to this method with practically no other means of treatment.[1]

As I have described so fully at other times the technique employed,[2] I will only say now that the plan, as we have carried it out at Marblehead, involves sufficient housing and proper conditions of institutional life, leaving out for the most part the usual elaborate facilities for hydrotherapy and electrical treatment. It includes a reasonable diet planned for the average and rarely modified for the individual.[3] It gives medicinal agents where these are manifestly needed; it supplies such amenities of life as may be found in music and in literary studies; it gives as much physical rest as seems required; it uses massage and physical exercises—these mostly corrective of the weak and relaxed physique of most nervous patients; it employs orthopedic corrective apparatus when the weakened muscles are unable of themselves to correct faulty carriage and the frequent condition of enteroptosis, and it gives work, not indiscriminately, but systematically, and in such measured doses as are indicated by the varying capacity of the individual.

Laying aside for a moment all physical considerations and all questions of mental or nervous complications, we must admit that most people are apt to be simple and happy when they are busy, and that they are almost sure to be complicated and involved when they are idle. I believe that a great many nervous patients fail to get well, and many organic invalids are made worse, because their lives have become disorganized from idleness and worry, as well as from pain, and that a long step will be taken toward a virtual cure when work within the capacity of the individual is made a part of the life.

The fatigue from which the subjects of nervous exhaustion suffer is one of the difficulties to be overcome. It can be overcome in most instances if the work, whatever its nature, is not pushed too hard, but is made so gradually progressive that there is never any strain or sudden effort required.

It should be easily possible to establish such industries in connection with the sanatoria and with most satisfactory results. I do not suppose for a mement that the usual sanatorium methods of treatment need be given up, for doubtless in some hands they are of the greatest use; but I believe that the sanatorium of the future

[1] I have had no experience with insanity, but I believe that work as a normalizer of life for these people promises excellent results and that the many institutions now proceeding along these lines will soon give valuable data.

[2] "Work Cure:" A Report of Five Years' Experience at an Institution Devoted to the Therapeutic Application of Manual Work, Jour. Amer. Med. Assoc., Jan. 1, 1910, liv, 12 to 14.

[3] We do not, as a rule, treat here such conditions as diabetes or nephritis requiring special diets.

will in an increasing degree become a training school where people may at once simplify their lives and strengthen their hands.

It is of vital interest to know that we have been able to establish at Marblehead, workshops which are self-supporting from their own products.[4] These shops are under the direction and constant supervision of skilled craftsmen, who accept the patients or pupils as assistants and apprentices. It is important to know that the system of occupation has proved a reconstructive and helpful measure in the lives of those who have overworked, quite as much as for those who have been too long idle. In these shops haste is discouraged. Patience and reasonable care are at a premium. Because of the careful supervision and because of preparatory work by experts, the products of the pupils have always been of a high order.

The plan works as well for persons of means as it does for those without resources. The patient having an abundance of money may easily make use of the sanatorium and of the workshops to his advantage; but most of the private institutions of the present day are founded and conducted in such a way that the person of moderate or small means cannot obtain their advantages. It is easy to understand that many professional people, dependent as they oftentimes are upon salaries, and who would otherwise be seriously handicapped from lack of funds and from the unhappy consciousness that they were spending too much, may under this system, in favorable cases, be brought to a stage of productive efficiency which makes possible their maintenance and at the same time serves the interest of the institution. As is well known, many professional and business people break down nervously and become dependent. Business and the professions say to the worker: "If you can measure up to our standards, we will keep you employed and pay you a salary. If for any reason you are not able to meet the requirements of your position, you must go. We cannot use you further." The economic considerations of occupation for the handicapped are far reaching. We may some day see large producing organizations working on this basis, providing at least a livelihood for many people who would otherwise be helpless and dependent.

We have employed at Marblehead the crafts of hand-weaving, wood-working, metal-working, pottery-making, and cement construction. The power looms of the world are turning out their enormous products, and we cannot, of course, hope in the slightest degree to compete; but there are little possibilities which the power looms miss in the way of novelties in design and in weave which the hand looms may profitably and wisely pick up. This we have

[4] We have recently moved into larger shops, so that at the present moment the industries are not quite self-supporting, but until this move the shops have for several years been on a paying basis.

shown many times. A design, for instance, for a small crib blanket having interesting and unusual patterns will for some months occupy our looms profitably. Meanwhile the designers must be considering another specialty to be ready as soon as the demand for the first design has ceased. Versatility in these lines is amply rewarded.

It must not be supposed for a moment that the untrained pupil can furnish these designs or prepare the looms for their weaving. But after a while the pupil may become so skilful in weaving that the products of his work amply justify the time and strength employed. Not infrequently a pupil may become proficient also in the most intricate and difficult parts of the work, becoming able to set up the looms and prepare them for unusual patterns.

The field of cement-working would, at first, seem to be an inhospitable one for such an institution. But, as a matter of fact, herein cleverness of management and design will count wonderfully. Cement-working, on a small scale, with carefully prepared moulds, is quite practical for untrained people, providing they are well directed. Cement, as everyone knows, is capable of a variety of excellent uses—first of all for building materials. The cement works are making quantities of tile and cement blocks, so far, unfortunately, mostly of crude design, and in the hopeless attempt to imitate stone.

After a year or more of experimenting we have discovered certain possibilities of color and texture in cement, which make it possible for us to produce brick and tile of unusual and attractive sorts, for which a fair price may be charged, and which can be made by hand better than in any other way. We are also making garden pots, garden seats, bird baths and the like in simple well-conceived designs, and which vary the monotony of the structural materials. We are even casting in cement small articles of special design for household or office use—such things as paper-weights, book-ends, ink-wells, pen-holders, etc. This is possible because the cement by special treatment is capable of a fine velvety finish, which makes it attractive, and because the color possibilities are greater than is commonly supposed.

It is in pottery-making that we have demonstrated most clearly the fact that practical industries may be founded upon the principles which we have outlined. We now have a pottery plant turning out a large and beautiful product, a pottery which is sold all over the country, and which has a large commercial field before it. This pottery is made by five people, two of whom were originally patients. Two of the others may well be called experts, and one of these has been under medical treatment part of the time, and owes his ability to earn a good living partly, at least, to the favorable conditions under which he works. Yet these five people produced in the last year and sold six thousand dollars' worth of

pottery, not a single piece of which was sold in any way except upon its merits, and in competition with other potteries on sale in various parts of the country. We do not often take new recruits into this department, because the work is of such a nature as to require careful handling.

Metal working I have tried with some persistence for a number of years, but I find that the physical exactions and the close work required make it, with difficulty, applicable to our special needs. I have also found it more difficult to sell the products.

Wood-working we have also tried persistently, especially wood-carving, and, while it is amusing and interesting, here also the close work seems to be more difficult to justify our using it indefinitely. Beautiful things may be made with the carving tools, but their sale is uncertain, and I do not recommend it as a craft for our special uses.

No doubt other men, with differing tastes and understanding, would make more of such things as metal-work and wood-carving, and perhaps use entirely different occupations. Of course, it must be understood that the success of any such work depends largely upon the enthusiasm and the skill of the directors and teachers. Without their coöperation and devotion to their work we could make no progress.

I shall hope as time goes on to develop a community of expert workers, partly recruited from among the patients and pupils, and producing goods of such quality as to command respect and interest anywhere, but depending for its life upon trained professional craftsmen. Into this atmosphere new pupils and patients may safely come, for it is a wholesome and hopeful atmosphere and one which can hardly fail to make a good background for the treatment of chronic illness of any sort, even of such kinds as do not allow of more than the slightest possible effort in the individual, because I believe that the happiness and development of those who are gaining and progressing under the system cannot fail to be contagious and inspiring. Here, as time goes by, we may develop conditions that will make such a community of the greatest human interest, and one which conserves in a large measure the faculties and abilities of many people who would otherwise have drifted on to all the unhappiness of chronic invalidism.

It is an amusing but suggestive fact that many people who are well are wont to remark, half in jest and half in earnest, after seeing the work which we are carrying on here, that they wish they might be just ill enough to warrant their coming into such a system which avoids so many of the complications and disappointments of the world outside, and yet which is no retreat, but rather a fair and reasonable meeting of the problems of life.

THE DIAGNOSIS OF THE FUNCTIONAL ACTIVITY OF THE PANCREATIC GLAND BY MEANS OF FERMENT ANALYSES OF THE DUODENAL CONTENTS AND OF THE STOOLS.[1]

By Burrill B. Crohn, M.D.,

VOLUNTEER ASSISTANT, PATHOLOGICAL LABORATORY, MT. SINAI HOSPITAL, NEW YORK.

The voluminous literature of later years has included many studies dealing with the functional activity of the pancreas, and the methods in vogue for ascertaining the state of efficiency of this gland. Until recent years the function of this organ was roughly judged by the occurrence of such a symptom as glycosuria or the appearance of bulky and fatty stools. The attempt to utilize for diagnosis the external secretion of the pancreas, resulted in testing the stool for the ferments supposedly originating in this gland, or the urine for the same ferments. More recently a method introduced by Boldyreff and elaborated by Volhard has been employed. This method consists of introducing an olive-oil test meal into the stomach and testing for regurgitated pancreatic ferments the contents withdrawn.

It is at once apparent that no one of these methods is a direct one, for in every instance the pancreatic ferments are obtained only after dilution with other body fluids or after passage through other organs. Within the last few years, Einhorn,[2] Hemmeter,[3] and Gross[4] have independently suggested the use of a catheter or a soft rubber tube to be introduced into the duodenum and to directly collect the pancreatic secretion at the time of its discharge from its duct. These methods afford a means, which, if practical, avoid the numerous sources of error of the hitherto circuitous ways of collecting material for purposes of testing. The following paper is founded upon the results obtained by analysis of duodenal and stool ferments in 27 chosen cases. These cases were all chosen because of a particular interest attached to the external secretion of the pancreas. For comparison, the findings in the duodenum of a normal control are defined and tabulated.

Method of Obtaining Duodenal Material. To obtain pancreatic secretion the Einhorn duodenal pump is used. This ingenious instrument was devised and perfected by Einhorn and has been used by him in many cases for collecting the duodenal contents. It consists of a vulcanized rubber catheter (one meter long) of narrow bore to one end of which is attached a small per-

[1] Read in part before the Eighth International Congress of Applied Chemists, September, 1912.
[2] Berl. klin. Woch., 1910, vol. xii, p. 522.
[3] Arch. f. Verdauungs-Krankheiten, 1896, vol. ii.
[4] Deutsch. med. Woch., 1909, xxxv, 706.

forated metallic capsule, and to the other end an aspirating glass syringe. My custom is to allow the patient to swallow the capsule and attached catheter (up to 80 centimeters) at eight o'clock at night, deglutition being assisted by the drinking of a little water. At twelve midnight, eight ounces of milk are drunk for the purpose of assisting the capsule to pass the pylorus during sleep. At 6.30 A.M. the same amount of milk is again administered. This latter milk serves as a test meal. Two and a half hours later the contents of the duodenum are aspirated. The catheter is slightly withdrawn until the point marked 80 centimeters is opposite the incisor teeth. At this point it is estimated that the capsule lies in the first part of the duodenum and opposite the point of exit of the pancreatic duct. Aspiration of the contents of the intestine is practised for five minutes, the volume and character of the resultant fluid being noted. This technique in all its steps, was adhered to rigorously throughout the course of this study.

The contents withdrawn are assumed to be duodenal contents if: (1) a radiograph showed the tube *in situ* in the duodenum; or, (2) if upon slowly withdrawing the tube, while aspirating, a distinct difference is noted between the contents obtained at the point marked 80 centimeters and the contents withdrawn after the metallic capsule is felt suddenly to enter the larger cavity of the stomach (56 centimeters). When the capsule lies in the duodenum, one obtains in the course of five minutes 10 to 40 cubic centimeters of golden-yellow, slightly acid or neutral, rather viscid fluid, with a more or less opalescent hue. This material can be aspirated only slowly. At first the contents present in the duodenum, 10 to 20 cubic centimeters, flow easily; then under continued negative pressure one obtains slowly, as it is secreted, a few cubic centimeters more of clearer golden yellow fluid. This material enters the aspirating syringe drop by drop, or rhythmically, every 20 to 30 seconds, with a rapid gush of 1 to 2 cubic centimeters of material. This latter phenomenon is probably due to a peristaltic acceleration of the secretions entering the duodenum at the moment and to the periodic expulsion of gastric juice.

The duodenal contents aspirated are almost always acid, due to the presence of the acid chyme, incompletely neutralized by the alkalinity of the pancreatic and biliary outflow. (The acidity was usually in normal cases 10 to 20 "acidity per cent.") The opalescence or milky appearance is similarly due to the expulsion through the pylorus of the incompletely digested milk (whey). When the capsule and catheter are withdrawn, until the former enters the stomach, a sudden gush of strongly acid milky material in great abundance is observed. This "retraction test," noted by Einhorn and by Hess[5] (the latter employing a catheter in infants for the

[5] Amer. Jour. Dis. Children, 1912, iii, 133 and 304.

purpose of obtaining duodenal juice) serves to differentiate duodenal from gastric contents, and is very important in cases where the biliary duct is obstructed, for here the absence of the golden bile in the duodenum complicates an otherwise simple maneuver.

CHEMICAL METHODS. Having obtained the contents of the first part of the duodenum, the presence and quantitative strength of the ferments is estimated. The fluid, after dilution with twice as much distilled water, was divided into two parts, one portion being kept acid (occasionally neutral), the other being made slightly alkaline with $\frac{n}{10}$ NaOH. The first portion serves for testing for amylase and lipase, the latter for the protease. The chemical methods as finally evolved are as follows:

1. DUODENAL FLUID. *Amylase.* In every one of several test tubes are placed one cubic centimeter of the fluid to be tested. Increasing amounts, from 0.5 c.c. to 6 c.c., of 1 per cent. starch solution[6] (Kahlbaum's soluble starch) are added to the successive test tubes, and then water to bring the volume up to 10 c.c.; incubation proceeds at 40° C. for one hour. The material is then tested by adding Lugol's solution drop by drop until an excess of iodine is apparent. The last tube in the series which fails to react for starch is the tube from which the reading is taken. The number of cubic centimeter of starch solution in this test tube multiplied by the dilution (three) gives the factor accepted as representing the amylolytic activity of 1 c.c. of duodenal contents in one hour.

Lipase. To 10 c.c. of distilled water are added 1 c.c. of the diluted duodenal juice, 1 c.c. of ethyl butyrate, 1 c.c. of toluol, and a drop of 1 per cent. alcoholic phenolphthalein solution; the whole is then made exactly neutral with $\frac{n}{10}$ NaOH and the total amount of fluid brought up to 25 c.c. After stoppering the flask, it is shaken forcefully for fifteen seconds and again brought to the exact neutral point.

A control test was always prepared, the duodenal juice of the control being boiled actively for five minutes before addition to the flask.

After incubation for twenty-four hours at 40° C. the two flasks are titrated for free acid, and the amount necessary to bring the control to neutral subtracted from the free acid in the test flask. The result multiplied by three (the dilution of the duodenal juice) denotes the lipolytic strength of the test material.

Protease. To test for alkali protease, Mett tubes, coagulated egg-albumen cubes, Fermi gelatin tubes (5 per cent. and 10 per cent.), and casein (Gross-Fuld method, as suggested by them for use in stool tests) are utilized.

2. STOOL. A 4 to 50 dilution of stool[7] in slightly alkaline distilled

[6] Prepared fresh every week; thymol as preservative.

[7] The diluted stool is used without being filtered, lest the strength of the ferments be attenuated in the process of filtration.

water is used as a basis for the estimations. The specimen of stool obtained is always a fresh specimen of that morning or a specimen obtained late during the night. No catharsis is used, as Ambard, Binet and Stadel[8] have demonstrated the marked inconstancy of results following purgation.

Amylase. The Hawk[9] modification of the Wohlgemuth method was adopted in a slightly different form.

Lipase and Protease. The same methods as exployed in testing the duodenal contents are employed.

TECHNICAL DISCUSSION OF TESTS.

There are few universally accepted methods for quantitative ferment analysis. The technique of this branch of biological chemistry is still in the evolutionary stage, and there are hardly two workers who can agree on methods, or on the interpretation to be derived from similar methods. A few remarks on the technical considerations of the tests appear warranted.

1. THE METHOD OF OBTAINING THE DUODENAL CONTENTS. At first the method used was to insert the duodenal pump in the morning and withdraw the contents after three or four hours. But it was found in most instances that this interval was far too short to allow the capsule to be propelled through the pylorus, and even a period of five to six hours during the day was insufficient. But when the tube was swallowed in the evening and the patient put at rest through the night, it was very exceptional to find the capsule still in the stomach in the morning. This delay occurred in only two classes of cases, pyloric stenosis and pyloric spasm associated with ulcer or hyperacidity.

In all instances the fluid removed was divided into two parts, one remaining acid, the other being made slightly alkaline with NaOH, and was then immediately iced. The tests were carried out five hours later. It was ascertained that in estimating amylolytic power, it was necessary to preserve the duodenal juice acid. In neutral or alkaline juice it was noted that the amylolytic ferment had apparently disappeared, due probably to the presence of active trypsin. When the material was preserved in its original acid state, the amylase could be kept for twenty-four to forty-eight hours with practically no loss of strength.

2. IDENTITY OF THE AMYLOLYTIC FERMENT. The question that frequently arose was whether one was dealing in the duodenal contents with salivary amylase carried through the stomach into the duodenum or actually with the similar pancreatic ferment.

[8] Compt. rend. Soc. d. Biol., 1907, p. 265.
[9] Arch. Int. Med., 1911, viii, 552.

Numerous tests of the gastric contents obtained in the course of removing the tube from the duodenum (and allowed to stand the usual five hours before testing) showed an absence of active amylase or only the slightest trace of this enzyme. So that it seems fair to assume that salivary amylase under these conditions, is destroyed by the presence of active pepsin, but that the pancreatic enzyme, even in the presence of gastric acid and pepsin, maintains its activity even for many hours.

In an article by Ambard, Binet and Stadel,[10] it was experimentally shown that the salivary amylase of the dog was only $\frac{1}{20}$ as strong as that of the pancreas; intestinal amylase only $\frac{1}{250}$ of the strength of pancreatic ferment. Extracts of the mucosa of the duodenum of dogs showed only the slightest amylolytic power, too faint to interfere with tests for pancreatic amylase. However, Roger[11] states that salivary amylase, even after its destruction by the gastric juice can augment pancreatic amylolytic activity, the "pouvoir zymotique" of the original ferment becoming a "pouvoir zymosthenique" after being acted upon by the gastric pepsin. It is very questionable whether this ability of the destroyed salivary enzyme is at any time sufficient to materially alter the figures obtained for pancreatic amylase.

3. Preservation of the Lipolytic Ferment. With regard to lipase, it was similarly found that this ferment was best maintained in the acid duodenal contents, being apparently protected in this manner from the destructive activity of the trypsin. In neutral and alkaline material lipase was demonstrated only in very small amounts after the fluid had been iced.

4. Preservation of the Proteolytic Ferment. The activity of the alkali-protease was best maintained in alkaline fluid. While even in acid meduim strong alkali-protease was demonstrable upon neutralization several hours later, yet this ferment was several times stronger in fluid maintained alkaline. The activity of the acid-protease (pepsin) in duodenal juice was not interfered with.

That autodigestion of pancreatic juice takes place very rapidly at high temperature has been convincingly shown by Nicolle and Pozerski.[12] These authors have demonstrated a very rapid weakening of all the ferments when the fluid is maintained at 50° C. Hence, the precaution of rapidly chilling the fluid when secured, is seen to be necessary in quantitative estimations of ferment strengths.

5. Identity of the Proteolytic Ferments. To return to a consideration of the alkali-protease found in duodenal content, one must consider that we are dealing with two ferments trypsin and erepsin. Erepsin originates from two sources, the duodenal mucosa (Cohnheim[13]) and from the pancreas (Bayliss and Star-

[10] Loc cit.
[11] Archiv. de Malad. de l'Apparat Digest. et de la Nutrition, 1909, iii, 509.
[12] Ann. de l'Inst. Pasteur, 1911, xxv, 336.
[13] Zeitsch. f. Phys. Chemie, No. 33, p. 451; No. 35, p. 134.

ling[14]). Schaeffer and Terroine,[15] experimenting with the excretion of an artificial pancreatic fistula in the dog, showed that in fluid in which trypsinogen was present but not activated by enterokinase, an ereptic ferment with peptone splitting properties was still present. Of the tests for alkali-protease, neither the Mett tubes nor the coagulated egg-albumen cubes are attacked by erepsin; nor are the Fermi gelatin tubes digested by erepsin. To establish this latter point, three fresh extracts of duodenal mucous membranes containing active erepsin (one cat, one dog, and one human intestine) were prepared after the method of Cohnheim. None of these extracts liquified gelatin even after three days.

These same extracts in their most concentrated form were tested for the casein digesting power of the intestinal mucosa. That the digestive power of these intestinal extracts is only a very slight fraction of the same power of the pancreatic secretion is seen by a comparison of the results obtained. Thus cat mucosa extract in dilution of 1 to 15, dog mucosa extract 1 to 140, human mucosa extract 1 to 10 digested 10 c.c. of 0.1 per cent. casein solution; normal human duodenal contents containing pancreatic secretion digests the same amount of casein in dilution up to 1 to 10,000. It seems therefore fair to deduce that the amount of erepsin present both in the mucous membrane of the duodenum and in the pancreatic secretion could not account for the active proteolysis of casein as found in duodenal contents. Hence, we seem justified in assuming that the pancreatic trypsin is the active factor here, and erepsin, while unquestionably present, yet of little moment in the tests, as carried out.

A similar process of reasoning seems justified in discussing the results of the stool examinations; for if the concentrated extract of normal duodenal mucosa digests casein in dilution of only 1 to 10, how can we explain the proteolysis of casein in dilutions of the stool up to 1 to 10,000 or 1 to 20,000, as frequently found, except on the hypothesis that it is the much more powerful pancreatic trypsin that is appearing in the stool.

Frank and Schittenhelm,[16] by means of complicated polypeptic splitting experiments, seem to demonstrate that the protease present in the stool is erepsin, rather than trypsin. It is difficult to harmonize their findings with such simple facts as the above. The occasional finding of a ferment in the stool which liquifies gelatin, would tend to confirm the impression that this ferment derives its origin from the pancreas. That bacteria do not simulate the results of the human ferments seems established by the fact

[14] Jour. Phys., 1903, No. 30, p. 61.
[15] Jour. de Phys. et de Path. Gén., 1910, xii, 884.
[16] Zeitsch. f. Exp. Path. u. Therapie, 1910, viii, 237.

that a case in which the pancreatic ducts has been proved to be closed gave complete negative results in both duodenal and stool analyses.

RESULTS OF TESTS OF THE DUODENAL CONTENTS OF A NORMAL PERSON.

One male adult, apparently in perfect health, furnished repeated specimens of duodenal contents.

The results on the different days are tabulated as follows:

TABLE I.

Amylase:

March 21,	1 c.c. duodenal juice hydrolyzes	6	c.c. of 1 per cent. starch solution in one hour.
March 28,	1 c.c. duodenal juice hydrolyzes	6	c.c. of 1 per cent. starch solution in one hour.
May 13,	1 c.c. duodenal juice hydrolyzes	10	c.c. of 1 per cent. starch solution in one hour.
May 14,	1 c.c. duodenal juice hydrolyzes	9	c.c. of 1 per cent. starch solution in one hour.
May 18,	1 c.c. duodenal juice hydrolyzes	24	c.c. of 1 per cent. starch solution in one hour.
May 10,	1 c.c. duodenal juice hydrolyzes	30	c.c. of 1 per cent. starch solution in one hour.
	Normal average	= 14.1	c.c.
	Normal limits	= 6–30	c.c.

Lipase:

March 21,	1 c.c. duodenal contents require	3.9	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
March 28,	1 c.c. duodenal contents require	3.6	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
May 13,	1 c.c. duodenal contents require	0.6[17]	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
May 15,	1 c.c. duodenal contents require	0.9	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
May 18,	1 c.c. duodenal contents require	1.9	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
May 26,	1 c.c. duodenal contents require	0.9	c.c. $\frac{n}{10}$ NaOH after twenty-four hours.
	Normal average	= 1.96	c.c.
	Normal limits	= 0.6 to 3.9	c.c.

Alkali-protease. Casein test:

March 21,	duodenal contents in dilution of 1 to	300	digests 10 c.c. of 1 per cent. casein solution.
March 28,	duodenal contents in dilution of 1 to	3,000	digests 10 c.c. of 1 per cent. casein solution.
May 15,	duodenal contents in dilution of 1 to	10,000	digests 10 c.c. of 1 per cent. casein solution.
May 18,	duodenal contents in dilution of 1 to	400	digests 10 c.c. of 1 per cent. casein solution
May 20,	duodenal contents in dilution of 1 to	3,000	digests 10 c.c. of 1 per cent. casein solution.
May 21,	duodenal contents in dilution of 1 to	1,000	digests 10 c.c. of 1 per cent. casein solution.
May 29,	duodenal contents in dilution of 1 to	1,000	digests 10 c.c. of 1 per cent. casein solution.
	Normal average	= 1 to	2,666
	Normal limits	= 1 to	300 to 1 to 10,000

Other Tests:

	Fermi, twenty-four hours.	Gelatin tubes, forty-eight hours.	Mett tubes.	Albumin cubes,
March 21	3.5 mm.	6.0 mm.	2 mm.	Slight rounding.
March 28	8.0 mm.	11.0 mm.	1 mm.	....
May 18	.....	.....	...	Much digested
May 20	5.0 mm.	10.0 mm.	1 mm.	All digested
May 26	8.0 mm.	14.0 mm.	..	....
May 29	10.0 mm.	15.0 mm.	..	....
Normal average	7.0 mm.	11.2 mm.		
Normal limits	3.5 to 10 mm.	6.0 to 15 mm.		

From a study of these tables it will readily be seen that quantitative estimates of the strength of pancreatic ferments obtained

[17] On one occasion no lipase was demonstrable.

from the duodenum of a normal man vary within wide limits. In practically every instance the three ferments tested for are found, and found in an active state. In only one instance was one ferment (lipase) absent. When tested for, rennet was always found. There is no method, however, of deciding whether this was gastric rennet or possibly a similar ferment from the pancreas.

PATHOLOGICAL CASES.

With this study of a normal adult male as a basis, further studies were undertaken on cases of interest because of pathological conditions. The cases observed are grouped according to similarity of diagnosis. The results obtained are presented in the accompanying table, with remarks:

GROUP I. *Cases of Cholelithiasis.* In these cases, the diagnosis of which was confirmed by operation, the ferments in the duodenum were found in an active state. A fairly wide range of variation is observed, yet in general the ferments are either normal or hypernormal in their activity. The exception is Case V, examined before operation. Here the absence of amylase and lipase suggested some abnormality of pancreatic secretion; at operation the head of the gland was found swollen and infiltrated to a marked degree. Bile flowed freely into the duodenum in all these cases; occasional admixtures of the bile with heavy viscid mucus indicated a condition of catarrhal cholangitis or cholecystitis.

GROUP II. *A Case of Acute Pancreatitis.* This case was one of acute pancreatitis with a diffuse abscess involving the body of this organ. The pancreatic ferments in the duodenal content were absent except for a faint lipolytic ferment. The identical condition was found on examination of the stool. As the head of the pancreas was found at autopsy to be preserved and the duct patent, it seems reasonable to conclude that an acute inflammation and degeneration had involved the entire gland, the result being that the ferments were either not elaborated, or as in the case of lipase, secreted but feebly. The corresponding result in the stool is of interest.

GROUP III. *Cases of Obstructive Jaundice.* The question here involved was: Is the pancreatic duct open, and is the pancreas secreting or not? In the first two instances (Cases VII and VIII) the duct was evidently open and active pancreatic ferments entered the intestine. These cases were one of intra-abdominal new-growth with evident masses throughout the abdomen, and one of post-operative stricture of the bile ducts. It is evident that the pathological condition affected the common bile duct but did not interfere with the patency of the pancreatic duct or ducts. In either case if the main pancreatic duct was obstructed it is evident that the accessory duct of Santorini maintained full compensation.

TABLE II.

		Amount.	Reaction.	Bile.	Duodenal Contents. Amylase.	Lipase.	Casein.	Fermi.	Mett.	Cubes.	Stool. Amylase.	Lipase.	Casein.	Fermi.
					GROUP A.									
Case I[18]	Cholelithiasis	7 c.c.	Acid	+	10 c.c.	0	1 to 5,800	—	—	—	—	—	—	—
Case II[18]	Cholelithiasis	15 c.c.	Acid	+	12 c.c.	6.3	1 to 12,000	—	0	—	—	—	—	—
Case III[18]	Cholelithiasis	35 c.c.	Acid	+	30 c.c.	10.0	1 to 1,000	3	—	—	0	0.1	1 to 700	—
Case IV[18]	Cholelithiasis	10 c.c.	Neutral	+	24 c.c.	3.6	1 to 18,000	10	2	+	10	0.25	1 to 50,000	2
Case V[18]	Cholelithiasis (before operation)	27 c.c.	Acid	+	0	0	1 to 5,000	10	—	—	—	—	—	—
					GROUP B.									
Case VI[18]	Acute pancreatitis	10 c.c.	Acid	+	0	1.8	0	—	—	—	0	0.2	0	—
					GROUP C.									
Case VII	Obstructive jaundice, new growth	12 c.c.	Neutral	0	4	2.4	1 to 4,000	3	0.5	+	0	0.3	0	0
Case VIII[18]	Obstructive jaundice, stricture	10 c.c.	Acid	0	30	0	1 to 4,000	{3 / 5}	—	—	0.5	1.0	0	0
Case IX[12]	Obstructive jaundice (*a*)	10 c.c.	Acid	0	0	0.5	0	—	0	—	0	0	0	—
	Duodenal sarcoma (*b*)	5 c.c.	Acid	+	4	3.4	1 to 600	3	0	—	2	0	1 to 200	0
					GROUP D.									
Case X	Hypertrophic cirrhosis of liver	25 c.c.	Neutral	+	27	—	1 to 18,000	7	0	+	8	1.5	1 to 3,000	0
Case XI	Hypertrophic cirrhosis of liver	50 c.c.	Acid	+	15	1.0	1 to 4,000	1	0	—	—	—	—	—
					GROUP E.									
Case XII	Duodenal ulcer	20 c.c.	Acid	+	20	—	1 to 6,000	—	—	—	++	1.5	1 to 5,000	—
Case XIII	Gastric neurosis	....	Alkaline	+	+	—	+ +	—	—	—	0	0	1 to 5,000	—
Case XIV	Gastric neurosis	8 c.c.	Acid	+	0	0	+	—	+	—	{1.0 / 5.0}	—	—	—
Case XV	Duodenal ulcer	15 c.c.	Acid	+	+ + +	0	+ +	—	—	—	—	—	—	—
Case XVI	Duodenal ulcer, hour-glass	3.5 c.c.	Alkaline	+	—	2.4	1 to 1,400	10	—	—	—	—	—	—
Case XVII[18]	Carcinoma of stomach	7 c.c.	Acid	+	9	5.4	0	—	0	—	—	—	—	—
Case XVIII	Achylia gastrica simplex	4 c.c.	Acid	+	3	8.4	1 to 4,000	3	0.5	Rennet neg.	6.0	0.1	1 to 30,000	—
					GROUP F.									
Case XIX	Diabetes (juvenile)	25 c.c.	Acid	+	6	4.5	+ + +	—	2	—	—	—	—	—
Case XX	Diabetes	9 c.c.	Acid	+	9	12.6	1 to 4,000	—	0	—	—	—	—	—
Case XXI	Diabetes (syphilis)	15 c.c.	Acid	+	30	2.7	1 to 6,000	{3 / 7}	0	+	1	0	1 to 700	—
Case XXII	Diabetes	3.5 c.c.	Acid	+	1.5	6.0	1 to 4,000	2.5	—	+	8	0.4	0	0
Case XXIII	Diabetes, milk diet } Fuller diet }	.... / 25 c.c.	Acid / Acid	+ / —	6 / 6	0 / 0.6	1 to 34 / 1 to 4,000	1.5 / 15	— / 1	— / +	—	—	—	—
Case XXIV	Diabetes, chronic pancreatitis (?)	3 c.c.	Alkaline	+	1.5	1.2	1 to 500	{5 / 11}	1	+	2.5	3	1 to 125	—
					GROUP G.									
Case XXV[18]	Retroperitoneal Hodgkin's disease	40 c.c.	Acid	+	0	5.6	1 to 4,000	8	1	+ +	—	—	—	—
Case XXVI[18]	Abdominal sarcoma	12 c.c.	Neutral	+	4	3.3	1 to 500	4	1.5	—	10	0.15	1 to 1,700	0
					GROUP H.									
Case XXVII	Chronic colitis	....	....	—	0	0.6	1 to 12,000	—	—	—	—	—	—	—

[18] Diagnosis confirmed by operation or autopsy.

In Case IX, on first examination the absence of all the ferments from the duodenum except a weak lipolytic ferment, and the absence of all the ferments from the stool, led to the diagnosis of complete pancreatic obstruction involving all the ducts emanating from the gland. On a second examination several weeks later, the results of both duodenal and stool analyses indicated some return of pancreatic ferments in the intestine. On autopsy, the head of the gland and the duodenum were found involved in a massive sarcomatous tumor. The ducts behind the new-growth were greatly dilated and distended with retained fluid. It seems probable that from time to time the pressure in the ducts was sufficiently great to force pancreatic secretion through the new-growth and into the intestine. This would seem the most likely interpretation of the later partial return of the characteristic ferments in the duodenum.

GROUP IV. *Cases of Hypertrophic Cirrhosis of the Liver.* Group IV represents the findings in two cases of hypertrophic cirrhosis of the liver. From the ferment analyses, the pancreas would seem to be secreting a fluid of high potentiality. The examination of the stool in the one case agrees with the findings in the duodenal material.

GROUP V. *Gastric Cases.* In this group is collected the data for various gastric diseases. As far as one can judge there is no evidence of disturbance of pancreatic secretion. It is of interest to note the absence of trypsin in a case of carcinoma of the stomach.

Case XVIII, one of achylia gastrica, requires a note. Repeated analyses of gastric contents showed the absence of both pepsin and rennin as well as all traces of acid. The pancreatic secretion is, however, active, all three of the ferments being present. Ehrman and Lederer,[19] employing the Volhard test meal method, found an active pancreatic ferment (trypsin) in these cases. In the duodenal contents, however, obtained by me in this case, no rennin was demonstrable. The question of the presence of a milk-coagulating ferment secreted by the pancreas is still an open one. The only facts bearing on this point in the living person are presented by authors who have tested the secretion collected from pancreatic fistulæ in diseased states. The results are contradictory; in a few instances a milk coagulating ferment being present, in others absent. With the direct method of collecting pancreatic secretion *via* the duodenum, no data on this point is at hand. In all instances with this means, some stomach contents are mixed with the duodenal fluid, and hence an individual test for pancreatic rennin is impossible. But in this instance gastric rennin, was repeatedly shown to be absent. Hence the inability to demonstrate in the duodenal material a milk coagulating ferment would speak for the absence of this enzyme in the secreting pancreatic

[19] Berl. klin. Woch., 1908.

gland. It is hardly probable that the absence of the enzyme from the gastric contents would result in a similar suppression in the pancreas, since all the other ferments known to be present in pancreatic secretion were actively demonstrable, and unaffected by the gastric condition.

GROUP VI. *Cases of Diabetes Mellitus.* In general it may be said that these cases do not show any variation from normal figures, all the three ferments tested for being found present and active. In only one instance was the reaction for amylase weak (Case XXII). In the instance of Case XXIII, on a strictly limited milk diet, the ferments were all only feebly present. A later examination, on a more liberal diet (oatmeal and milk) revealed ferments of greater strength.

Case XXIV was of interest, being a case of diabetes mellitus in a female adult with a distinct history of cholelithiasis and abdominal attacks indicating pancreatitis. The stools in this case were bulky, grayish-white, and frequent. Metabolism studies indicated, even on a restricted diet, a loss in the stools of 54 per cent. of the fat, and 29.4 per cent. of the nitrogen intake, corroborating, so far as our studies of metabolism would indicate, pancreatic insufficiency.

The duodenal findings demonstrated a very scant secretion into the intestine, though of high potentiality. The stool in the same case showed active ferments, though only weak protease.

From the study of these cases it seems probable that the external secretion of the pancreas plays no role in the pathology of diabetes mellitus. This conclusion should not be interpreted to exclude the presence of a chronic pancreatitis with changes in the islands of Langerhans in these cases, for it can be conceived that these changes might be present and yet the external pancreatic secretion be uninfluenced, at least not demonstrable by our present methods. No idea of the internal secretion of this organ is obtainable from these analyses.

GROUPS VII AND VIII. *Miscellaneous Cases.* The ferments are present and active, except for amylase, which is absent in two instances. The failure to demonstrate this ferment was probably due to faulty technique in the early tests.

REMARKS. The original intention of this study was to determine (1) the limits of ferment activity in the normal duodenum; (2) possible variations from these normal limits in pathological cases; (3) to determine in how far the analysis of the ferments of the stool gave an indication of pancreatic functional activity.

In regard to establishing a standard for the strengths of the ferments as normally secreted, Table I represents the limits of variation. It would seem that the pancreatic ferments show fluctuations of strength from day to day even under identical conditions, but that such fluctuations may be said to be within reasonable bounds. However, the occasional failure to detect amyl-

ase or lipase in seemingly normal secretions must be noted. These ferments show the greatest variability in strength, and may apparently be occasionally absent. The protease is the most constant and is always present in the duodenum when the pancreatic duct is open. In spite of the arguments against casein as a test of trypsin alone, I would hold that erepsin, though present, is never sufficiently strong to interfere with the test as an index of pancreatic trypsin.

Of the pathological cases examined, the case of acute pancreatitis shows decided diminution in the activity of the pancreatic ferments. The pancreatic gland was found decidedly diseased at autopsy. In Case IX (the case of sarcoma of the duodenum) the ferments were absent from the duodenum on one occasion; also absent from the stool. The diagnosis of complete blocking of the ducts was confirmed at autopsy. In Case V, on account of the absence of two of the ferments from the duodenal juices, a disease of the pancreas was expected. At operation the duct was found patent, but the pancreatic gland was found swollen and inflamed.

In Case XXIV the metabolism studies indicated pancreatic disease. The ferments were found strongly present; the amount of secretion into the duodenum was, however, very scant.

The variability of the strength of these same ferments as tested in the stool is far greater than in the duodenum. The occasional absence of a ferment is a more frequent occurrence. In general where these enzyme are strongly present in the duodenum they are also demonstrable in the stool. The protease is here no longer reliable as an index of pancreatic trypsin. For in Cases VII, VIII and XXII, though a strong reaction for trypsin was obtained in the duodenal contents, this enzyme was not demonstrable in the stool (casein and gelatin tests). However, in Case IX, when the protease was absent from the duodenum, it was also absent from the stool; and when it reappeared in the former, it also reappeared, though weakly, in the latter. We may conclude that a positive test for trypsin in the stool signifies an open pancreatic duct; a negative test does not necessarily imply that active trypsin is no longer being secreted into the duodenum.

The important question that rises is: Can this method of estimating the enzyme strength of duodenal contents be utilized for the diagnosis of pancreatic functional activity? It seems certain that it is reliable for ascertaining the patency or non-patency of the ducts of this gland. More experience with cases of disease of the pancreatic gland proper is necessary before it will be definitely known whether the method is applicable to the diagnosis of the functional activity of this organ. From the few cases offered in the series, it would seem that the method lends itself to prognosticating qualitative and quantitative variations in the strength of the pancreatic external secretion.

It is well known that very little idea of gastric function is pos-

sible from quantitative tests of the ferments elaborated by the human stomach, and yet this does not preclude the possibility of more reliable information of the pancreatic gland being obtained by this method of testing. It will remain to be demonstrated whether moderate pathological changes in the tissue of the gland will evidence itself by variations in the titer of the enzymes of the external secretion.

The study of a vast clinical material, with a uniform method of collecting and testing the duodenal contents in these cases, will be necessary to establish the further value of this method.

Since writing this article for publication, the author has noted the appearances in the literature of the experiences of Frank[20] with this same method. Frank succeeded in obtaining duodenal contents in 60 per cent. of the persons he attempted. The cases were chosen at random and suffered no pancreatic disease. The duodenal contents in all these instances showed active alkali-protease where tested for. The other ferments were not investigated. The inability of Frank to obtain the duodenal material desired in 40 per cent. of his essays is probably due to too short a time being allowed for the metallic capsule to enter the duodenum. This is obviated in my series of cases, by passing the pump in the evening and allowing the entire night to elapse before aspirating the desired material. Even then, more than one attempt is sometimes required before success is attained. The procedure is a mild one, and only exceptionally objectionable to the patient.

The sincerest thanks of the author are offered to the physicians and surgeons of the attending staff of Mount Sinai Hospital for the privileges of studying clinical material in their wards; to Dr. Samuel Bookman, for kind suggestions and hearty coöperation. and to the House Staff of the Hospital (more particularly Dr. Mahler) for general assistance throughout the course of this work,

A STUDY OF EMPYEMA, WITH SPECIAL REFERENCE TO THE FEASIBILITY AND IMPORTANCE OF DEPENDENT DRAINAGE.[1]

By T. Turner Thomas, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY AND ASSOCIATE IN SURGERY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

The large number of operations which have been done in recent years has added much to our knowledge of the pathological changes

[20] Archiv f. Verdauungs-Krankheiten, 1912, xviii, 121.

[1] Read before the College of Physicians of Philadelphia, November 6, 1912.

which have taken place and the mechanical conditions which have arisen in connection with the various disease organs or tissues on account of which the operations have been performed. Our opportunities for the study of a pathological condition are much improved when during the operation it becomes necessary to remove the diseased organ or tissue, as in appendectomies, gastrectomies for ulcers or carcinoma, or in operations for the removal of other tumors. Even when nothing is removed a free exposure of the affected part is often obtained, so that practical observations can be made from sight and touch. Yet from the large number of operations which have been done for empyema we have learned little in this way. The opening made in the chest wall is too small for inspection of the diseased parts within, in the presence of the escaping pus, and the finger is too short for palpation. Our efforts, of necessity, have been confined chiefly to bacteriological examinations of the pus evacuated and to a study of the relation of the pus collection to the preceding infectious condition of the lung, as pneumonia or phthisis. Robinson[2] says that the bacteriology is of interest in prognosis, but of no significance as regards treatment. All cases should be recognized promptly and drained freely, reëxpansion of the lung being the main purpose from the start. Most surgeons will probably agree with these statements.

In a previous paper[3] on empyema I employed an illustration of a formalin-hardened cadaver specimen, from the department of applied anatomy of the University of Pennsylvania, of an empyema from which the pus had not been evacuated during life. The possession of this specimen is the result of an accident, it having been selected for injection with formalin as one in which the normal relations and conditions of the abdominal and thoracic organs should be found, and I used it for the first time to illustrate how easily a large empyema could be overlooked on inspection. I have come to the conclusion that it was worthy of a more careful study and that it might yield valuable practical information concerning empyema in general. When making a study of conditions in the dead body we usually obtain our material from the dissecting or postmortem room. This kind of a specimen could hardly be obtained from either. It must be specially prepared, and one must know that the unopened empyema is in a body before he prepares it, unless, as in this case, he happens to find it by accident after he has injected the body with formalin. The number of empyemas that find their way into the postmortem room unrecognized and unopened is probably very small, and those that do are usually so mutilated before the empyema is recognized that the preparation of a formalin specimen of this kind would be impossible.

[2] Boston Med. and Surg. Jour., 1910, clxiii, 561.
[3] Internat. Clinics, 1906, 165; iii, 150.

The first incision and manipulations necessary to expose the empyema would render the injection of the formalin ineffective, and would distort the relations of the soft structures to each other. In the dissecting room the conditions would be similar or worse

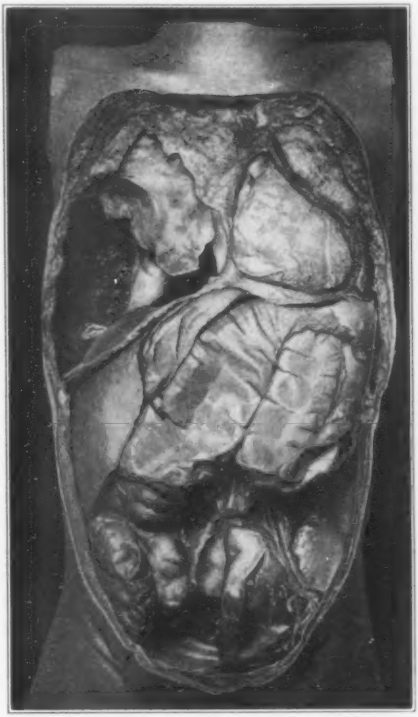


FIG. 1.—Formalin hardened cadaver specimen of an empyema which has been completely circumscribed by firm adhesions above between the lung and chest wall. A small portion of the lung, narrower than appears in the illustration, remained adherent to the diaphragm. The costophrenic sinus is much wider than normal from the pressure of the pus, while on the opposite side it is almost obliterated. The heart pushed to the left looks larger than it actually is because abnormally uncovered by the left lung which is crowded posteriorly and to the left. The placing of the drainage opening at the bottom of the normal pleural cavity (see Fig. 2) would have been easy and safe in this case, as it proved to be in the three cases in which it was so placed. The large intestine is much distended and the liver distorted and depressed by the pressure of the pus.

for the preservation of a similar specimen. If an opening had been made during life, such changes would have taken place that would have rendered the specimen less valuable, because we are most interested clinically in the empyema before the pus has been evacuated. Fig. 1 shows that there existed here the large common

and typical empyema, that giving marked and superficial dulness extending from the bottom of the pleural cavity a variable distance upward and merging below on the right side with the liver dulness. The displacement of the heart and liver are also typical.

A bacteriological examination of the pus debris remaining in the specimen was made by Dr. Rivas, of the University of Pennsylvania. He found in it leukocytes, lymphocytes, two kinds of bacilli, and a diplococcus. One of the bacilli was acid-fast, and suggested the tubercle bacillus. This was confirmed by a longitudinal section of the affected lung. The specimen had been lying in a strong formalin solution for about eight years, so that the pus debris from which Dr. Rivas made his examination had undergone such change as not to permit an exact bacteriological report. He concluded that the pus had been the result of a mixed infection. The most striking and important feature in connection with the specimen, in my opinion, is that the empyemic cavity, although a large one, is distinctly and firmly circumscribed below by the junction of the diaphragm and chest wall and above by adhesions between the lung and chest wall, so intimate and continuous that the line of cleavage between the two cannot be seen. I have seen a formalin preparation of a tuberculous empyema in which there were no adhesions between the two pleural layers, the lung lying completely collapsed against the spine. The probability is that in the latter there had developed a communication between a bronchus and the pleural cavity, resulting in a pneumothorax in the presence of a slight tendency toward adhesion formation. In my specimen there could be found no evidence of such a bronchial communication after a careful search of all surfaces presenting on the empyema, which was aided by a removal of a longitudinal section of the lung, about 3 inches wide, and extending the whole length of the lung. The firm and extensive adhesions sharply circumscribing the empyemic cavity were probably due to absence of a bronchial communication, and the fact that there was added to the tuberculous a pyogenic infection; the latter having a greater tendency toward adhesion formation than the former. This does not mean that tuberculous infection cannot produce the condition exhibited by this specimen. There is much vagueness in the literature concerning the existence of and the part played by adhesions in empyema. Many writers ignore their existence; some refer to bands of adhesions; while others seem to think their existence is largely a matter of chance. If they developed extensively in the presence of a mixed tuberculous and pyogenic infection, as in this case, I believe they are almost certain to occur in the acute pyogenic infections, including the pneumococcic, in which pneumothorax is rare. Indeed, the burden of proof should not be upon him who says that such adhesion formation is the rule, but upon him who says that it is not.

The empyema in this specimen extended from the bottom of the normal pleural cavity upward, anteriorly at one point as high as the second rib and posteriorly in a rather broad channel as high as the apex. It was one continuous cavity and no bands of adhesions crossed it. It was thoroughly walled off on all sides: above by close and firm adhesion between the lung and chest wall, and below by the union of the diaphragm and chest wall. I have based my study of empyema chiefly upon the character of the adhesion formation in this specimen, and upon the assumption that it is the rule in acute empyema. Many of the accepted teachings in connection with empyema, according to my judgment, have either taken no account of this feature or have not given it sufficient recognition. I have drawn some inferences from my study that I look upon more as suggestions than conclusions. The main definite conclusion I would draw is that dependent drainage in empyema, which calls for an opening as low as the eleventh rib or to the top of the twelfth rib in most cases, is not only feasible but comparatively easy and safe.

This massive type of empyema is frequently referred to as the unencysted or general, which implies that the pus is free to flow into all parts of the affected pleural cavity. The specimen strongly contradicts this conception, and shows, in my opinion, that practically all acute empyemas are encysted and localized by surrounding more or less firm adhesions, as in an appendicular or other abdominal abscess, or the small so-called localized empyema. The latter is localized, but probably no more so than the large one.

Morison[4] says that the collecting effusion is first observed in the region of the fifth interspace, that is, diagonally farthest from the fixed point of the lung at its root, and that the reëxpanding lung last touches the chest wall in the same region. For this reason he makes this the point of election for the drainage opening. According to my experience most empyemas extend from the bottom of the pleural cavity, as in this specimen, a variable distance upward. I believe that the fluid begins to collect not about the fifth rib, but at the bottom of the normal cavity. Donaldson[5] says that "the fluid products in pleurisy gravitate by their weight to the lowest portion of the cavity of the pleura and then gradually rise." The last part of the lung to reëxpand is probably that about the drainage opening, at whatever level it may be, where the external atmospheric pressure acts longest and to the best advantage. Considerations based upon this specimen suggest the following conception as to the conditions developing in and about an empyema. Most pneumonias affect the base of the lung, therefore the resulting pleural effusion should begin at the base of the pleural cavity. But let us suppose that the infection involves a higher

[4] Trans. Med. Chir. Soc., Edinburgh, 1907 to 1908, vol. xxvii.
[5] Pepper's System of Medicine, iii, 487.

portion of the lung and reaches the pleura on the corresponding portion of the external surface of the lung. If adhesions develop between the visceral and parietal pleuræ, here, there can be no empyma, because there is no space in which the fluid can collect. If no adhesions develop the excess of fluid which results from the pleurisy falls immediately to the bottom of the pleural cavity and prevents adhesions between the surfaces over which it continues to fall. It should collect first in the costophrenic sinus, pushing the lung here away from the chest wall and diaphragm and the latter two from each other, as in the specimen. I would again agree with Robinson when he says that he is "not in sympathy with Fowler, who says that adhesions may occur in the costophrenic angle, raising the level of the bottom of the cavity so that the drainage need not be at the lowest point." Such adhesions might develop after a drainage opening had been made, but are not likely before. The accumulating fluid pushes the serous surfaces apart, but sooner or later where they are in contact above the pus collection and around the whole lung the approximated surfaces develop adhesions, weak at first but gradually growing firmer. In this way the pus becomes walled off all around by adhesions between the lung and chest wall, and probably some part of the diaphragm. This walling off is much more likely than with the average pus collection in the abdominal cavity, because in the pleural cavity the pus is less likely, from the nature of the cavity and the usual position of the patient, to move about. For the same reason a pelvic infection is less likely to give rise to a general peritonitis than one in the appendix or gall-bladder region. The cadaver specimen shows clearly that such a walling off occurred in this case, and that it usually occurs in empyema is strongly indicated by the fact that when a patient is changed from the sitting to the recumbent position there is little or no variation in the upper line of dulness. Movable dulness is probably rare in empyema, except perhaps in the early stages, before the adhesions have become strong enough to withstand the pressure of the pus under the influence of gravity. Donaldson says: "Once formed, these effusions (of pleurisy) are but slightly movable and but little displaced by the varying positions of the patients, unless the quantity be very great and no adhesions or bands have been made." He also says, "The serous transudations of hydrothorax always occupy the most dependent portion of the cavity." In other words, the fluid in the latter moves about under the influence of gravity. In an empyema the weight of the pus might cause a slight change in its position by pressure against the more or less soft lung. We know that the upper line of dulness in the sitting position is not straight but curved, the curve varying more or less, and that it does not change materially when the patient is placed in the recumbent position. The varying curve of this line is probably dependent

upon the position occupied by the patient during the development of the limiting adhesions. The absence of movable dulness as determined by percussion before and after a change in the position of the patient should be a sufficient guarantee that the pus has become circumscribed by adhesions in any given case.

The adhesions probably developed early and became stronger as the quantity of pus, and therefore its upward pressure increased, so that they held the adherent surfaces of the lung to the chest wall while the under surface of the lung removed from the chest wall was being pushed upward, the pus therefore reaching its highest level a variable distance from the chest wall. Above this level, especially when the pus collection is large, the percussion note is often hypertympanitic—Skoda's resonance—particularly in the first and second interspaces anteriorly. In the formalin specimen the pus at one point reached as high as the second rib, so that in large collections the first and second ribs or interspaces anteriorly cover about all of the lung above the pus that comes as close to the skin surface. Posteriorly and above the first rib anteriorly it is covered by a much thicker layer of muscles and other tissues. The inference to be drawn is that the lung is more tympanitic anteriorly in the first and second interspaces because it is nearest to the surface here. Skoda's resonance is explained by a retraction and relaxation of the lung from its elasticity and the upward pressure of the pus. This implies that the lung is being floated upward by the pus causing it to become relaxed. It has seemed to me that retracted and relaxed lung must be more or less functionless according to the degree of collapse, resulting from the relaxation. If its air cells are full of air and functionating it can hardly be collapsed. The support which the lung obtains from its firm attachment to the chest wall in its whole circumference must aid it in resisting the upward pressure of the pus and in keeping its air channels open for respiration. The lung is not floating in the ordinary sense on the fluid pus, and therefore largely collapsed and functionless, but is probably trying to maintain its function with the aid of the extensive firm adhesions, the atmospheric pressure exerted through the trachea, and with the aid of an increase in the capacity of the thorax produced by the auxiliary muscles of respiration. The portion of the lung tissue caught between this air pressure above and the pus pressure below is probably compressed and condensed, not relaxed. In the normal lung conditions the tidal air is only about one-third of the air contained in the lung. Necessity may now increase the proportion of the tidal air in the functionating portion of the lung, so that the hypertympany may be the result of overdistended, not relaxed lung. Auer and Meltzer[6] say that the actual necessity of respiratory

[6] Jour. Exper. Med., 1911, xiv, 569.

function for the mere maintenance of life amounts only to a small fraction of the normal respiration, and that the extent of the changes of gases occurring in normal respiration with a closed thoracic cavity exceeds greatly the need for the maintenance of life, since normal respiration is provided with an abundance of factors of safety. Necessity demands in an empyema that any still functionating portion of the lung shall work to its full capacity. It is generally agreed that the lung on the sound side is doing compensatory work, why not any sound lung on the affected side? That it probably does so is strongly indicated by the fact that a patient can live with a large empyema on each side, and the fact that he can live under these circumstances, indicates that the pressure of the large collection of pus on each lung is being largely offset by the extensive firm adhesions in the whole circumference of each lung. These began to develop early and resisted with increasing firmness the increasing pressure.

If a considerable portion of the lung is so functionating then it follows that this portion is occupying about its normal proportion of the thoracic cavity, and the portion which formerly occupied the space now represented by the empyemic cavity must be more or less compressed and condensed below the functionating portion. The adhesions were developed in the early stages between surfaces about in their normal relations to each other, and they probably continued to hold these surfaces together against the pressure developing later from the accumulating pus. This means, in my opinion, that the adhesions will not seriously hinder the reëxpansion of the lung after the pus has been evacuated, and that the cavity is to be filled by reëxpansion of that portion of the lung which presents upon or projects into the cavity. The adherent surface of the lung is about where it should be when the lung is fully expanded, and therefore the adhesions should not be broken up to favor reëxpansion of the lung.

Elsberg[7] reported some interesting facts concerning pneumothorax, observed in experimental work on dogs. Many of the dogs either died suddenly as soon as an opening was made into the pleural cavity, or a violent expiratory dyspnea ensued, soon followed by rupture of the mediastinal septum, double pneumothorax, and death. While most of the dogs stood well, a small opening in the chest wall, sudden heart stoppage or dyspnea, and death followed in some instances. The larger the opening, however, the more likely is the occurrence of serious interference with the respiration. In almost all the animals in which the size of the opening approached or exceeded that of the diameter of the trachea, when the dog was lying on its back, dyspnea and death followed. It made no difference in what part of the chest wall the opening was made. The

[7] New York Med. Rec., 1908, lxxiii, 846.

cause of the rapid death seems to be the development of the double pneumothorax. If a dog will die of a total double pneumothorax a man should. But it is now known that a double empyema may be opened on both sides at the same operation and the patient live. Hellin,[8] after a study of 113 cases collected from the literature and 1 of his own, makes some very interesting statements in this connection. He says: "The question of a double empyema is closely related to that of a double pneumothorax. *A priori*, one would expect that a simultaneous opening of both pleural cavities would prove fatal. At first it was considered best to open the second pleural cavity after the first had been closed. (An interval of one hundred and fifty days was allowed to elapse in one case.) But compelled because of the severity of the constitutional condition, it was gradually found that the interval between the opening of the two cavities could be shortened until both were opened at the same operation. The skeptic can convince himself that the classical theory born of a fear of a double pneumothorax is unfounded, since the patients do not cease to breathe in spite of the two opened pleural cavities." Hellin in his case found that the cyanosis occurring during anesthesia disappeared on the opening of the pleural cavities. In experiments on dogs he noted that some of the animals survived even after the collapse of both lungs if the opening in the first cavity was closed. Auer and Meltzer showed that while from the opening of the pleural cavity in the dog, collapse of the lungs, dyspnea, and death occur, if the opening were closed after the collapse of the lungs had occurred, the dog would continue to live. Only an open pneumothorax causes dyspnea. When the cavity was closed, even though the lungs have recently collapsed, an inspiration will cause some distention of the lungs and an inspiration of air into them. An expiration will cause a compression of the lungs and a removal of the carbon dioxide. Hellin[9] inferred from his studies that a total double pneumothorax was not necessarily fatal, but that, as in caissons, it is chiefly in the suddenness of the change of pressure that the danger lies. But he assumed also that simultaneous opening on both sides of a double empyema gave rise to a total pneumothorax on both sides. Fabrikant[10] asks if we may not hope that under these circumstances pleural adhesions will prevent collapse of both lungs. The formalin cadaver specimen gives an affirmative answer to this question. It is possible that the adhesions in the early stages may break down at some point and admit air to any open part of the pleural cavity above; but this would probably be very rare, if it occurred at all. The empyema specimen which represents probably the great majority of this massive type shows

[8] Berlin. klin. Woch., 1905, xlii, 1415.
[9] Archiv f. Klin., 1907, lxxxii, 866.
[10] Deutsch. Zeitschr. f. Chir., 1911, cviii, 584.

clearly why a patient can live after the simultaneous opening of a double empyema on both sides. The air is admitted not into the whole pleural cavity of each side, but into only the strongly walled off pus cavities, which are now extrapleural in the sense that an appendiceal abscess becomes extraperitoneal. The atmospheric pressure can now exert its effect only upon the surface of the lung presenting on the empyema which is buttressed against a threatening collapse by the strong adhesions which before the opening was made protected it against the severe pus pressure. The atmospheric pressure is always the same, but the pus pressure will probably vary with the quantity of pus present, so that the immediate effect of the drainage opening on the lung will probably depend upon the difference in the two pressures one way or the other. It is my impression that I have seen patients breathe better after the operation when they are resting quietly in bed, and that I have seen cases in which the breathing was not as good.

The fear is sometimes expressed that the rapid evacuation of the pus following the usual opening made by the resection of a small portion of a rib will be accompanied by a dangerous change of pressure on the surrounding displaced organs, especially the heart. Hellin feared this and advised that all empyemas, unilateral as well as bilateral, be aspirated immediately before operation or one or two days before, in order that a too sudden change of pressure may not take place. I have seen a fairly large number of empyemas opened, but I have never seen such a danger threaten, and I believe that it is very rare. With each outflow of pus from the opening on expiration there immediately follows an inrush of air on inspiration to take the place of the pus evacuated, until when the pus is all evacuated its place has been taken by air at a pressure of about 15 pounds to the square inch. There is therefore probably no great change of pressure, and certainly not a sudden one. The ominous loud noise made by the air rushing in through the opening with each inspiration is in reality an indication not of danger, but of safety. As already stated, Hellin observed in his case of double empyema that the cyanosis occurring during narcosis, disappeared after the empyemas had been opened on both sides.

I have operated upon three and possibly four of the so-called localized or encysted empyemas. Since I believe that the usual large variety is in practically all cases circumscribed by adhesions, I believe that these names do not properly distinguish the small ones. The status of these cases has not yet been decided. I would suggest that they are practically all interlobar or between the diaphragm and under surface of the lung and that that is the reason for their small size, the pus becoming walled off by adhesions before it can get out of the fissure or the space between the diaphragm and under surface of the lung.

In connection with these small empyemas, Musser[11] emphasized the importance of firm and deep pressure in the intercostal spaces along the fissures and along the margins of the diaphragm or upper borders of the liver, to develop tenderness indicating the presence of small empyemas between the lobes of the lung or between the lung and diaphragm.

Murphy[12] says that many of the cases diagnosticated as abscesses of the lung are actually the result of empyemas communicating with a bronchus. Those diagnosticated as lung abscesses are very likely small and covered by more or less lung tissue, that is, they are interlobar. The pus breaks into the lung and ultimately finds its way into the air passages because it cannot well extend in any other direction. Depending upon the depth in the fissure at which it develops, the pus may or may not extend along the fissure and come to lie directly under the chest wall when a small area of absolute dulness could be detected. It may fail to do so because of its depth, when it will be covered by a layer of lung tissue, the dulness be relative, and air sounds be detected over it. The fissure is so oblique that it would be practically impossible to evacuate some deep collections by finding the fissure through an opening in the chest wall, and usually in such cases it is necessary to reach the pus by going through the lung tissue covering it, first shutting off the pleural cavity if necessary by suturing the lung to the chest wall in the circumference of the opening in the wall. The presence of sufficient adhesions here would render this unnecessary. When the pus collection is in the outer portion of the fissure directly under the chest wall the lung in the circumference of the empyema will be firmly adherent to the wall. In my 4 cases, I had 3 of the superficial variety and 1 of the deep. Small empyemas may develop between the base of the lung and the diaphragm, as already stated, but I have had no experience with this variety. It is said that these small empyemas frequently develop on the external surface of the lung between it and the chest wall. If they do it probably will be in an adherent portion enclosing a non-adherent area. The probability is, however, that such a condition is rare, and if a careful examination is made it is likely that in these cases the pus collection is close to some part of one of the main fissures. Robinson believes that most of these cases are peripheral abscesses of the lung. He refers to 2 cases which he saw at autopsy and 3 upon which he operated, in all of which the evidence as he interpreted it pointed to their having originated in abscesses of the lung. This evidence consisted in the fact that he found lung parenchyma devoid of pleura on the pulmonary side of the cavity. He expected to find the inner wall of the empyema made up of visceral pleura.

[11] Jour. Amer. Med. Assoc., January 5, 1907, xlviii, 24.
[12] Ibid., 1898, xxxi, 281.

I believe with Robinson that the pus will not often break through the pleura into the lung substance in the usual large empyema, that between the parietal and visceral pleuræ. As already stated, I believe that an interlobar empyema remains small because the pus becomes circumscribed soon from the fact that it cannot easily spread itself out in the fissure. Gravity probably has little effect on it, and the movement of the apposed pleural surfaces normally is probably slight. As soon as it becomes walled off the pus can increase in quantity only at the expense of the lung which surrounds it. When it can no longer make room for itself by pushing the lung aside it will destroy it as it will destroy any other tissue which confines it, even bone. The pleura will probably first become necrotic and then the lung tissue and the process will continue until the pus finds an exit or kills the patient. Sometimes it will burrow externally through an interspace between the ribs. The lung is the weaker tissue, however, and therefore evacuation through the trachea, is the more common. We should not expect to find the pleura intact on the visceral side if the empyema has existed long enough to destroy it, and in many cases it probably has, by the time the empyema is opened, because this variety is usually the most difficult to detect.

The main purpose of any general study of empyema should be to improve our methods of treatment. In recent years we have had a number of valuable contributions looking toward this end. The main discussion seems to centre about the question of the method of drainage, and the consideration which has received most attention is that of the influence of the atmospheric pressure admitted through the drainage opening. Most cases get well sooner or later from drainage in the usual way, but in a considerable number the closure of the opening and cavity is much prolonged, or they may not close at all. Murphy[13] says that before the surgeon makes an opening into an empyema he should be reasonably certain that it will close later. He has discarded operation in all cases in which there is not an external opening or a communication with a bronchus. In other words, if air has not already gained entrance into the empyemic cavity through an external or an internal opening he will keep it out. He aspirates the pus and injects into the cavity a few drams or ounces of a 2 per cent. formaldehyde and glycerin solution, repeating the procedure at intervals of a few weeks as the effusion re-collects, until it has entirely disappeared. The fact that Murphy employs it in all cases, with the exceptions mentioned, attests its value and alone makes it a method which will be widely tested when it has been fully placed before the profession. As yet he has spoken of it only briefly in the discussion of papers by others. The formalin is said to render the cavity sterile and to favor the absorption of the

[13] Section on Surgery of the American Medical Association, 1909, p. 921.

exudate. Tennant[14] tried the method, but in one case it failed him and a resection of a rib was done. It is the ideal method for combating the ill effects of atmospheric pressure on the external surface of the lung, and if it comes into general use there will be fewer cases calling for the severe Estlander or Schede operations. But it has not yet received general approval, and the prevailing treatment is that with drainage.

Many devices and methods of obtaining drainage with the exclusion of air from the cavity have been offered, and recently von Eberts[15] and Robinson have added valuable contributions on this phase of the subject. Except for a brief attempt in one of my cases, which was soon discontinued, I have not as yet had any experience with these methods. It seems to me that before we can determine, with satisfaction, the relative value of suction or siphon methods of drainage we must first know approximately the limit of rapidity with which an empyemic cavity may be permitted to become obliterated. We are dealing with an abscess the walls of which are infected, and few surgeons will risk efforts at disinfection by irrigation. The rule is to permit the cleansing to be done by the natural processes after effective drainage has been instituted. In most cases in which drainage is employed in the usual way, without the use of suction, the cavity cleanses itself spontaneously and is obliterated by the expansion of the lung, sooner or later. Fraley[16] reported a study of 500 cases of pleurisy treated at the Pennsylvania Hospital. About one-fifth of them were empyemas. No case was cured in less than four weeks. The average was ninety days, in which column were found one-third of the cases. All but 6 were cured in four months or less, and these were severely complicated. The shortest duration of convalescence obtained by Robinson with his method of rib trephining and suction drainage was four weeks, although in the one fatal case, in which death occurred two weeks after operation, the lung was fully expanded as shown at autopsy. We might argue with some force, therefore, that about four weeks are necessary, under the most favorable conditions, for the disinfection necessary before the cavity and drainage opening can close permanently. But the conditions vary. The degree of firmness with which the lung has become fixed in its compressed condition will affect the rapidity of expansion. The character of the infection will affect the rapidity of spontaneous cleansing, as will the presence of necrotic tissue in the wall of the empyema. According to Schädler, quoted by Hellin, the average duration of a unilateral empyema was fourteen and one-half weeks, in children nine weeks. Hellin says that the death rate in 1335 cases of unilateral empyema was 22.4 per cent.

[14] Jour. Amer. Med. Assoc., August 15, 1908, p. 572.

[15] Von Eberts and Hall, Montreal Med. Jour., June, 1910, 513; Annals of Surg., 1910, lii, 502; Ibid., 1911, liv, 59; Jour. Amer. Med. Assoc., 1912, lix, 264.

[16] Amer. Jour. Med. Sci., May, 1907.

or 299 deaths. The mortality in the double empyemas was 0.1 per cent. Robinson evidently made a careful study of other methods of suction drainage than his own, and of them he says: "It is well known to those who have performed rib resection and introduced tubes protected by rubber collars, rubber dam, adhesive plaster, lanolin, zinc ointment, gutta percha, cement, and other agents that leakage is of frequent occurrence and that at best it can only be prevented by the most painstaking and continuous efforts." In his discussion of this subject at the meeting of the American Medical Association in June, 1912,[17] and at the meeting of the Pennsylvania State Medical Society, September 26, 1912, Robinson said that he now confines the use of suction drainage to only the most carefully selected cases.

It is an interesting fact that while the atmospheric pressure soon after the usual drainage opening is made is probably as great in the empyemic cavity as that exerted within the lung through the trachea, because the drainage opening is usually as large or larger in diameter than that of the trachea or larynx, in most cases the lung will expand later and obliterate the cavity. This is the more interesting when we take into consideration the fact that to the external pressure must be added the resistance of the normal elasticity of the lung and that of the inflammatory thickening of the inflamed pleura and adjacent lung tissue. In many cases this result will be accomplished in about four weeks without the employment of negative tension from suction drainage. Yet is is obvious that the lung can be expanded only by the atmospheric pressure coming through the trachea. The internal pressure in some way must gain on the external pressure. I have in several cases introduced my finger through the drainage opening at the time of the operation to find that I could not feel lung tissue or only a small portion of it. It was being held beyond the reach of the finger by the external atmospheric pressure exerted through the drainage opening. In 1 or 2 cases I have introduced the finger at intervals later to find that the surface of the lung could be felt to be approaching the opening. To my mind there is only one satisfactory explanation for it. The atmospheric pressure within the empyemic cavity must, in some way, be gradually diminished, so that the internal pressure can act to better advantage in expanding the lung. Otherwise the lung never could expand. In other words, the effect of the drainage opening usually employed is to provide more or less imperfectly, a negative tension within the empyemic cavity. We are all familiar with the sound made by the air which passes through the opening on inspiration during the after treatment even in the presence of a pus-soaked dressing. I observed in one of my cases that this sound ceased soon after the operation, perhaps in a few days, and in that case the cavity and sinus were closed in five weeks. I saw at the Philadelphia Hospital some years ago an

[17] Jour. Amer. Med. Assoc., 1912, lix, 272.

empyema patient who had been operated on about two and a half years before. The drainage opening was more than an inch wide at that time. There was no sound in that case from the passage of air in or out, probably because the opening was so large. I could look through it into the cavity, and when I saw the case again a year later, as far as I could judge, no progress had been made toward the obliteration of the cavity and a cure. I have observed that the sinus is not long in closing after the sound made by the inrush of air on inspiration has ceased. Whether the sound ceases because the cavity has almost closed or the cavity closes more rapidly because the air has ceased to enter is uncertain, but it has seemed to me that if the entrance of air could be prevented the average case would be cured much sooner than it is. The small number of cases which I have had has prevented me from following up this idea as I would wish.

In my opinion the size and position of the opening have an important bearing upon the results of the operation. Elsberg showed that the size of the opening was an important factor in connection with the effects of experimental pneumothorax in dogs. If the opening made in most operations remained afterward as large as when made, I think that in many cases the lung never would expand, because it would be practically as large as that of the trachea or larynx, so that the external atmospheric pressure would remain constantly as great or greater than the internal pressure. It seems to me that the external opening must become smaller than the internal, or the tracheal diameter, before the lung can expand. After the usual operation the falling in of the soft tissues contracts the opening, which is further filled by the walls of the drainage-tube, and the lumen of the tube and the space around it are more or less choked up continually by the escaping discharge and fragments of fibrin. The air already in the empyemic cavity is becoming absorbed, and if a smaller quantity passes in than is being absorbed the external pressure on the lung is being diminished, so that the internal pressure coming through the trachea remaining the same the lung slowly expands. The excision of several ribs may be advisable to get nearer to the bottom of the cavity, but not to provide freer drainage. Through-and-through drainage by two openings with a tube in each and one higher than the other, in my opinion, is worse. The higher opening will always be admitting air freely, because the pus will be escaping entirely by the lower, so that the upper will be a strong factor in preventing reëxpansion of the lung. The term free drainage in connection with empyema has not the same meaning as with abscesses in other parts of the body. In many abscesses an incision is made from one end of the abscess to the other, and lays the cavity wide open. The Estlander operation for chronic empyema provides such an opening, and the result shows what is to be expected from it. The free admission of atmospheric pressure permanently prevents reëxpan-

sion of a large portion of the lung, which causes a marked sinking in of the side of the chest and a corresponding loss of lung function. The small opening usually employed in acute empyemas, if placed at the bottom of the cavity, would provide drainage quite free enough for the average case.

Robinson says that in the early stages, with the drainage opening at the bottom of the cavity, suction drainage will not be necessary. I am, particularly, trying to show that this will be true for most cases. In 2 cases I made the opening by resecting a small portion of the tenth and in 3 cases the eleventh rib near the spine. By dividing the intercostal tissues in the latter to the top of the twelfth rib practically the very bottom of the cavity was reached. I did this because of observations made on the formalin specimen, which shows that in that case at least there would have been no difficulty in making such an opening, and I found in my cases that it was about as easy and safe as resecting the sixth or seventh rib. A small puncture wound was made in about the seventh interspace or where the aspirating needle demonstrated pus. A somewhat rigid probe or a long grooved director, curved at the end, was then introduced through this opening and the end made to seek the lowest limit of the empyemic cavity, which usually corresponded to the bottom of the normal pleural cavity near the spine. The curve permitted the end of the instrument to be turned toward the surface where by careful palpation it could be felt by the finger outside over the corresponding interspace, usually the eleventh. A vertical incision was then made over this area, the eleventh rib exposed, and a small portion of it excised in the usual way. The probe or grooved director was then pushed outward through the pleura if it had not been already opened and a closed hemostatic forceps introduced at this point. The finger introduced through the opening thus made feels the twelfth rib below and the diaphragm at the bottom of the cavity. A drainage-tube is introduced after extending the opening by incision to the top of the rib below. A suture or two may be used to diminish the size of the opening slightly, but free drainage must be the first consideration. During the operation I have placed the patient in the prone position advised by Elsberg, and have found it satisfactory. In one case, as I was about to make the preliminary incision for the introduction of the probe, I happened to look at a clock and I concluded to time the operation. When the drainage-tube was in and the gauze dressing applied about four minutes, not more than five, had elapsed. With such an opening the empyema will be perfectly drained in almost any position the patient is likely to occupy. The shoulders will probably be higher at all times than the opening, the advantage increasing the more nearly the patient assumes the sitting position. The opening is at the bottom of the narrow space between the diaphragm and chest wall, so that all of the discharge will constantly gravitate toward it and will tend to prevent the entrance of air

in so far as it continues to fill the space in and around the tube. Usually I have not been greatly concerned about fragments of fibrin choking the tube, because I have felt that the drainage was free enough around the tube, and through it around any fibrin that became lodged in it. At any rate it will give no more trouble than with a higher opening. When we consider that we can in a short time evacuate the accumulation of weeks through the ordinary aspirating needle, it becomes evident that not much space is necessary with such a low opening for the continuous evacuation of the discharge as it forms. Nor have I been concerned about the falling in of the drainage-tube, since it is usually directed upward as well as inward, and would have to travel against gravity to get inside; and if it did so, would be kept by gravity at the opening so that it could easily be fished out with a forceps

Agnew[18] applied the principle of dependent drainage in old empyemas with persistent sinuses, but maintained through-and-through drainage with a tube passed frm one opening to the other. Ashhurst[19] employed the same method of drainage from the beginning, and says: "I have seen a number of cases in which this plan has been systematically carried out with complete success." It seems reasonable to assume that the lower opening drained all the pus in Ashhurst's cases, since pus could escape from the upper opening (the patient usually occupies the semirecumbent position from the beginning and soon the upright) only if the cavity were full of pus, when the plan would hardly have been regarded as a complete success. The important point demonstrated by Ashhurst, in my opinion, is that an intercostal dependent opening only large enough apparently to pass the drainage-tube gave satisfactory drainage. But we have many surgeons who employ such an opening usually in the sixth or seventh interspace, especially in children. If the drainage is satisfactory through such an opening it ought to be better with the opening in the eleventh interspace. Only a scarcity of cases has prevented me from trying the low intercostal opening.

Some surgeons make efforts to remove fragments of fibrin at the time of operation. I have felt some concern about them because they were in a pus cavity and were probably made up of necrotic material. I had one experience, however, that modified this opinion. On introducing my finger through the drainage opening I found the pleural surfaces, parietal and diaphragmatic, covered uniformly as far as the finger could reach with a soft layer of fibrin about an inch in thickness, which could easily be swept off with the finger. It seemed obvious that the whole surface of the cavity was so covered and that it was all infected material. As it could not be removed I watched the after course of the case with much interest. The sinus closed and the patient was discharged in

[18] Agnew's Surgery, vol. i, pp. 344 and 345.
[19] Principles and Practice of Surgery, 1893, sixth edition, p. 410.

about five weeks. The layer of fibrin gave no trouble. It did not escape through the drainage opening unless it liquefied, which is unlikely. It is more probable that it remained and became organized into a thickened pleura. I did not discover such a deposit on the pleural surface in any other case. It suggests that in the pleural cavity we have the serous, serofibrinous, and fibrinous varieties of inflammation, as in other serous cavities, and that the thickened pleuræ found in some old cases at operation may be due to the organization of such deposits. Thomson and Miles[20] say: "Even in comparatively recent cases the pleura is thickened and covered with masses of flaky lymph, which may be an inch thick. In some cases of long standing this fibrinous exudate becomes organized and the pleura is greatly thickened."

In those troublesome cases in which the affected lung fails to expand after a prolonged period the last resort is a thoracoplasty, by the Estlander or Schede method, with or without removal of the thickened pleura covering the exposed part of the lung. Since the latter will not expand to obliterate the cavity the ribs overlying it are removed, permitting the weakened chest wall to fall in against the lung. The operation is frequently a severe one and the resulting deformity marked. The lung remains permanently collapsed in large measure, which with the sinking in of the chest wall produces a condition which is far from desirable. Robinson believes that these operations are too often employed in cases which are by no means beyond the possibility of reëxpansion. I believe that this is true. Ochsner[21] has made an important contribution to the treatment of these cases. In 14 cases he injected the cavity with Beck's bismuth paste, and all but 2, which were still under treatment, were cured. He has used it only in cases with sinuses, although, he says, it has been suggested to aspirate the pus in the empyema and to inject the paste into the cavity through the cannula. While the method appears to be decidedly better than thoracoplasty, it would hardly be advisable to employ it to the exclusion of the usual drainage method, which results in a cure in most cases, with almost if not complete reëxpansion of the lung. Any paste retained permanently must be at the expense of the non-expansion of a corresponding portion of the lung. The cases calling for the Ochsner method, or thoracoplasty, are usually chronic not in the sense that they have long existed without being opened, but are cases which were opened in the acute or subacute stages and became chronic while waiting for the lung to expand. It is likely that in the chronic cases the lung has expanded considerably since drainage was begun, and therefore will require a much smaller quantity of the paste than if injected at the time the pus was first evacuated.

(To be continued.)

[20] Manual of Surgery, fourth edition, ii, 318.
[21] Annals of Surgery, 1909, l, 151.

REVIEWS

PROGRESSIVE MEDICINE. A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES, AND IMPROVEMENTS IN THE MEDICAL AND SURGICAL SCIENCES. Edited by Hobart A. Hare, M.D., Professor of Therapeutics and Diagnosis in the Jefferson Medical College of Philadelphia. Assisted by LEIGHTON F. APPLEMAN, M.D., Instructor of Therapeutics in the Jefferson Medical College of Philadelphia. Vol. iv, December, 1912, pp. 381; 62 illustrations. Philadelphia and New York: Lea & Febiger.

IN the final number of *Progressive Medicine* for 1912, Edward H. Goodman contributes, for the first time, the article on diseases of the digestive tract and allied organs. Readers of *Progressive Medicine* will recall that for the past few years this section has been written by R. S. Lavenson, whose carefully prepared and interesting articles will long be remembered as models of this type of critical medical literature. The selection of Goodman as Lavenson's successor will meet with general approval, not only because of his well-known work along the lines of gastro-intestinal diseases and physiological chemistry, but also because of his present admirable contribution, which makes it evident that the high standard set by his able predecessor is destined to be maintained.

Goodman covers thoroughly the more recent and interesting problems in relation to diseases of the gastro-intestinal tract. Among the subjects which he discusses is the analysis of gastric contents, the pathological physiology of the stomach, gastric ulcer, and carcinoma. Under the intestine some of the newer subjects touched on are the intestinal flora, chronic intestinal stasis with special reference to the work of Lane, and cecum mobile. After devoting a few pages to the liver, he discusses at more length chronic pancreatitis, functional tests of pancreatic insufficiency, and a number of other interesting pancreatic conditions. His entire article occupies 124 pages.

Under diseases of the kidneys, John R. Bradford, takes up particularly hemaglobinuria, the functional activity of the kidneys, movable kidney, albuminuria, and cystic disease of the kidney.

The subject of genito-urinary disease is well handled by Charles W. Bonney. After discussing affections of the kidneys, ureter and bladder, he turns his attention to the prostate, urethra, and numerous miscellaneous conditions.

In a contribution of 108 pages, Joseph C. Bloodgood writes most instructively on shock, anesthesia, infections, tumors, and the surgery of the skin, muscles, fasciæ, tendons, and bones and joints. Although it is impossible to mention in detail the many subjects he considers, attention should be drawn particularly to his discussion of preventive surgery, anesthesia and blood pressure, epithelial tumors, benign connective-tissue tumors, myositis, and the operative treatment of bunions.

The concluding section of 80 pages on practical therapeutics by H. R. M. Landis, deals not only with a number of the newer remedies, but also covers such subjects as antidiphtheretic serum, vaccines, climate, and heliotherapy.

The entire volume is of unusual interest and forms a valuable addition to the preceding volumes published during the past year

G. M. P.

PSYCHOTHERAPY. By JAMES WALSH, M.D., Ph.D., Dean and Professor of Functional Nervous Diseases and of the History of Medicine at Fordham University School of Medicine, and of Physiological Psychology at the Cathedral College, New York. Pp. 806. 34 illustrations. New York and London: D. Appleton & Co., 1912.

IT would have been impossible for Dr. Walsh, who is equally well known for his extra medical knowledge, to have produced anything else but an interesting and philosophical work. It is, of course, very well written, and, as would be expected, full of historical references. The most interesting part of the book, to the reviewer at least, is the part upon the history of psychotherapeutics.

The plan of the work is to take up the general question of psychotherapy in the history of medicine, in which everything that has a bearing is discussed, such as signatures, pseudoscience, mental healing, nostrums, talismans, charms, and faith cures. In the next section, on general considerations, the influence of the mind on the body, body on the mind, secondary personality and hypnotism are taken up. In the third the individual patient is discussed and his general work, pleasures, and in fact his whole day is critically analyzed and suggestions given. Then comes the chapter on general psychotherapeutics, in which the principles are laid down, this being followed by a section on general adjuvants and treatment, such as exercises, suggestion, aversion of mind, habit, and then follows special psychotherapy which takes up almost every disease under the sun. It is, as the author states, the only complete book on psychotherapy.

It would be impossible to review a work of this kind in full

because to do so it would be necessary to write a smaller one. Suffice it to say that it is such a work as should be in the hands of the patient as much as in the hands of the physician, for it is optimism that Dr. Walsh preaches. "Nothing is as bad as it seems, and if you only make up your mind to it and cheer up, everything will be better." For example, if the general practitioner who buys this book wants to look up even such a hopeless disease as hemiplegia, he is met with the statement that Pasteur had a stroke at the age of fifty and yet lived for twenty years, and did his best work after it. What could be more cheerful and promising? Specifically, Dr. Walsh's advice is excellent. He believes in common sense methods and takes advantage of any legitimate means that he can in treatment. He believes in the judicious use of hypnotism. One fault of the work, if there is a fault, is the fact that there is a great deal of repetition, but this no doubt is the purpose of the author, for he perhaps means that if anyone wants to look up what should be done under a certain disease he will find complete advice. Necessarily if every disease is discussed in the same manner repetitions must occur. Were it not for this, such a book could be written in about 200 pages instead of 800.

The average neurologist, however, who will expect to find a discussion of psycho-analysis, as taught by Freud, will be met with disappointment, for Freud is dismissed in a trifle over a page. Dr. Walsh evidently believes that Freudism is only a fad, and classes it with osteopathy and Eddyism. Like osteopathy and Christian Science, however, it will remain and grow stronger. It is to be regretted that such an important subject should be dismissed so lightly and with such evident scorn. The reviewer is by no means an ardent Freudian. He believes, however, in common with those neurologists who have paid attention to it, that there is a great deal in psycho-analysis, and that it is by no means a fad and that it will live. It has been the style since Freud's work to condemn those who have either taken up or who favor it, rather than to discuss psycho-analysis on its merits, and the criticisms have been somewhat caustic and by no means always tinctured with wisdom. The basis of the whole criticism is that Freud believes that most neuroses have as a cause some previous experience which in the majority of cases is sexual. Its critics always state that it is abhorrent to them to discuss sexual matters with the patient, and it does no good. As a matter of fact, the trained psycho-analyst does not discuss sexual matters with his patient because he wants to. He does it because he finds that he has to, and that the average normal person as well as the nervous patient has a great many ideas about sexual matters which need straightening out, and very often the basis of such a neuroses may be a previous sexual experience or sexual thought which the patient

many not be at all aware of. The truth of the matter is that the average doctor, in common with other humans, wants to get the most results with the least amount of effort, and that he very rarely desires to face the situation, especially if it is disagreeable. In our education sexual matters are always placed in the background, for it is a crime to discuss those things which are always before us, and it seems that it is a greater crime for the doctor to discuss them than for anyone else, and yet the doctor is supposed to heal! How long will we have to wait until, like Tanner in Shaw's *Man and Superman*, we will state facts as facts and truths as truths, and live accordingly? T. H. W.

BLUTKRANKHEITEN UND BLUTDIAGNOSTIK. LEHRBUCH DER MORPHOLOGISCHEN HÄMATOLOGIE. Von Dr. med. OTTO NAEGELI, Privatdozent an der Universität Zürich. Second edition. Leipzig: Veit & Co., 1912.

THE second edition of Naegeli's "Blutkrankheiten und Blutdiagnostik" will be welcomed by all who are interested in the study of hematology. It has been very largely rewritten and much enlarged, and many new colored plates have been added.

Those familiar with the first edition of this work will find that the author still adheres largely to the teachings of the Ehrlich school. That he is not a passive follower is well known; many of his personal observations appear here for the first time. However, the reader is not presented with the facts to support one view alone, but a fairly impartial presentation is made, and from these the author draws his conclusions. In matters of controversy, the opposing interpretations of morphological or tinctorial abnormalities are stated.

Technical procedures are well discussed. Practically all of the stains which are useful in the study of the blood are given; the methods of staining are described, together with the best fixatives for a given stain. This applies to the staining of blood films and of sections of tissue as well. To the laboratory worker, one drawback is evident; the method of preparing the stain is seldom stated. Instead, one is advised to buy the prepared staining mixtures, usually from Grubler.

In the new edition the viscosity of the blood is fully considered. The inclusion of many observations by the author adds greatly to the value of the discussion.

The section on the red blood corpuscles, like other parts of the book, has been brought fully up to date. The pathological alterations of the red cells are taken up in detail, and there is an adequate description of each, well illustrated in the colored plates. As

examples, ring bodies, Howell-Jolly bodies, and chromatin dots may be cited. Normal and pathological regeneration of the erythrocytes is described in the embryo, in the normal adult, in anemias, in the embryos of animals, and in experimental anemias.

The discussion of the leukocytes is equally complete and illuminating. The various types of leukocytosis are considered in detail.

The blood findings in disease are well presented. This is true not only of the diseases affecting the blood-forming organs primarily, such as chlorosis, pernicious anemia, the leukemias, but also of all diseases in which changes in erythrocytes, leukocytes, or platelets are usually met. Fewer additions are to be found in this part of the volume, though here, as elsewhere throughout the treatise, personal observations of the author are in evidence.

It is a pleasure to record the fact that the author, unlike most of his German-speaking colleagues, has not been content to ignore the foreign literature. His pages teem with references to French, Italian, English, and American authors. In fact, his thorough mastery of the literature of his subject explains the high value of the work the author has produced. Excellent bibliographies are appended to each chapter.

In a review it is impossible to give an adequate idea of the scope of a volume. Suffice it to say that the title of the present work expresses very clearly its contents. If any important morphological studies of the blood have escaped the notice of the author, the reviewer has failed to detect the fact. That he has placed insufficient stress on certain contributions is inevitable. The observations of Wright and his co-workers upon the origin of blood-platelets is a case in point, in the opinion of the reviewer.

Naegeli's "Blutkrankheiten und Blutdiagnostik" is unhesitatingly recommended as a valuable aid to the study of hematology.

R. S. M.

A Cross-section Anatomy. By Albert C. Eycleshymer, B.S., Ph.D., M.D., Professor of Anatomy, St. Louis University, and Daniel M. Schoemaker, B.S., M.D., Associate Professor of Anatomy, St Louis University. New York and London: D. Appleton & Company, 1911.

In recalling the advances in gross human anatomy during the last twenty-five years, the introduction and wide use of two methods of study—hardening *in situ* and cutting frozen sections—stand out conspicuously as most productive factors. The publication by Professor His, in 1878, of his studies on bodies hardened by injections of chromic acid solutions, and, later, the dissemination of his findings by means of models cast from his preparations,

wrought a revolution in visceral anatomy and exposed many current errors regarding the form and relations of important organs. Scarcely less important, although not so generally appreciated, was the appearance, in 1872, of Braune's splendid work, "Topographisch-Anatomischer Atlas. Nach Durchschnitten an gefrorenen Cadavern." Although by no means the pioneer in this important field of anatomical observation—for, among others, Pirogoff had produced his monumental work twenty years before—Braune did more than any of his predecessors to awaken an interest in sectional anatomy and to make available the results of such study.

The introduction of formalin as a preserving and hardening fluid marks a new era in anatomical technique, especially in connection with frozen sections. This combination, first used by Gerota in 1895, is now so highly valued and widely employed by anatomists the world over, that it is justly regarded as indispensable. Thanks to these improvements in anatomical methods, our present understanding of the form and relations of the various parts of the body, especially the viscera, is far more accurate and complete than when dependence was so largely placed on dissociation. Moreover, the advantages of combining the older and newer procedures, that is dissecting the sections of the formalin hardened bodies, are so pronounced for certain lines of work, that the method is now often followed, yielding preparations in which the parts may be separated or assembled, like the pieces of a picture puzzle.

Appreciating the necessity of cross-sections as a means of acquiring accurate notions concerning topographical relations, Dr. Eycleshymer and his associates, Drs. Schoemaker and Smith, have undertaken to make such important data available, when access to frozen sections stored in anatomical instituties is impracticable. Indeed, in no other field of anatomy do careful drawings offer so satisfactory a substitute for actual preparations as in the one under discussion. How adequately these gentlemen have fulfilled their self-appointed task, is shown by the admirable atlas before us.

The work consists of four divisions: (1) Introduction, giving an interesting historical sketch of the development of sectional anatomy and a description of the material and methods used in the preparation of the plates; (2) illustrations of the cross-sections, with explanatory text and key-figures; (3) topography of the organs, including a critical review of the position of the most important, and (4) bibliography.

The atlas comprises 102 quarto plates, of which 87 picture the upper surfaces of 113 consecutive cross-sections, supplemented by 14 key-figures and one plate illustrating the vertebral levels of the thoracic and abdominal viscera. Of the 113 cross-sections, 19 are of the head and neck, 29 of the trunk (including a series of five sections through the pelvis of a female subject), while the remaining ones are of the extremities, the upper limb contributing 26 and the lower 39 sections.

Recognizing the importance of thorough orientation for an adequate understanding and appreciation of cross-sections, the authors have wisely taken special pains to supply the necessary correlation by a generous series of admirable key-figures. The care with which these have been prepared is one of the features of the work calling for particular commendation. Thus, not only is the surface level of any given head-section seen by a glance at Key-figure 1, but reference to the following two figures shows in detail the relations of the section to the superficial and deeper structures, the third figure being a mesial sagittal section of the head, on which are indicated the planes of all the sections. Moreover, these key-figures are not merely arbitrary sketches, on which the approximate levels of the sections have been drawn, but are based on reconstructions from the sections themselves and, consequently, insure accurate correspondence between the details of the sections and those of the keys.

The sections throughout the work are on a uniform scale of four-fifths natural size, thus affording ample space and size for even small details without resorting to plates of inconveniently large dimensions. Accuracy in the illustrations was secured by tracing the surface of each section directly on a sheet of thin glass, subsequently transferring the outlines to paper by retracing under transmitted light. The technical excellence of the finished drawings, as reproduced in the printed plate, is most gratifying, for these are not only clear and exact, but represent the textures of the cut structures with so much fidelity and artistic feeling, that one recognizes a likeness, not merely a diagram.

The difficult problem of labelling the many structures to be seen in the sections has been solved very satisfactorily. The necessary leaders, in some cases fourscore or more in number, are definite and distinct, being carried, with judgment and taste, beyond the margins of the sections. At the end of each leader, the name of the indicated structure, printed in neat legible type, supplies the means of ready identification. In addition, each leader is consecutively numbered, so that the index and text references may be conveniently located. The nomenclature of the plates is uniformly the B.N.A., but, where necessary, the synonyms in the older terms are given in the descriptive text.

The value of the plates illustrating the head-sections passing through the brain has been materially increased by avoiding the uninteresting repetition of the details of the two sides. This advantage has been gained by doubling the number of actual sections on one side of the head, so that while the upper surface of the section of the usual thickness is shown on one-half of the plate, the other half is devoted to the upper surface of the intervening section. In this way, the views of the sectioned brain have been doubled, without adding to the number of the plates. By skilful

use of shadows, the relations of the levels of the two surfaces are made evident.

It is, perhaps, in the study of the cross-sections of the trunk, that the value of the reconstructed key-figures will be most appreciated. These key-figures comprise a series of four plates, representing the body from the shoulders to just below the trochanters. Although only approximately two-fifths natural size, and, therefore, about one-half the scale of the sections, they are sufficiently large to supply satisfactory orientation. The first depicts the skeleton in relation to the surface contour, and shows the planes of the 26 sections and their vertebral levels. The second key-figure, done in colors, exhibits the relations of the cross-sections to the muscles of the antero-lateral body wall, the skeleton being shown in outline. The third key-figure, also in colors, gives the relations of the planes of the sections to the heart and great vascular trunks, and to the brachial, lumbar, and sacral plexuses. The fourth key-figure, made entirely by reconstruction, represents the thoracic and abdominal viscera and displays their mutual relations, as well as their relations to the levels of the sections and to the skeleton.

In order to insure an understanding of the five cross-sections of the female pelvis, by Dr. Carroll Smith, which supplement the trunk series of the male body, a key-figure, representing a mesial sagittal section of the pelvis, is provided. This figure was obtained by assembling the actual cross-sections and cutting them sagittally, in this manner securing accurate correspondence between the details of the sections and those of the key. In consequence of a full bladder and distended rectum, the uterus is somewhat elevated.

The cross-sections of the extremities also are elucidated by excellent key-figures, based on reconstructions from the sections themselves. The two key-figures of the upper limb, from the lower border of the insertion of the pectoralis major to the hand, and about two-fifths natural size, exhibit the relations of the sections to the surface, skeleton, muscles, bloodvessels, and nerves, and serve to recall the form and disposition of the structures usually studied in dissections. The same assistance is provided for the lower limb by two reconstruction keys of the thigh and leg and by two additional ones of the ankle and foot.

The division of the work relating to the topography of the thorax and abdomen is contributed by Dr. Peter Potter and embodies the results of his arduous reconstructions of ten adult bodies of male negroes. The measurements, as to vertebral levels, were taken from sections of formalin hardened bodies and recorded in a comprehensive table. The average levels, deduced from these observations, were utilized to construct the interesting and useful plate, in which the thoracic and abdominal organs are shown, from in front and in colors, projected in accordance with their average relations to the spine.

The bibliography assembles the titles of almost one hundred publications bearing upon sectional anatomy. The wealth of anatomical details contained in the atlas is made available by an excellent index, by means of which the exact location in the plates of any structure may be readily found. The index also serves to correlate the new and old terminology, by giving both names where confusing differences exist.

An accurate knowledge of the topographical relations of many parts of the body is, manifestly, so important, that not only the serious student of human anatomy, but also, and perhaps even more, the clinician should heartily welcome this important addition to his means of acquiring such information. As a piece of bookmaking, the work is admirable and a conspicuous example of the results obtainable by coöperation of authors, artist, and publishers. All of these are to be congratulated; moreover, this congratulation may be extended to American Anatomy, on the production from its ranks of a contribution of such high merit. G. A. P.

SALVARSAN IN SYPHILIS AND ALLIED DISEASES. By J. E. R. McDENAGH, F.R.C.S., Surgeon to Out-patients, London Lock Hospitals. Supplement to System of Syphilis. By POWER and MURPHY. 150 pages, 11 illustrations and 3 plates. London, Oxford University Press, 1912.

THIS work fills an important place in the literature of syphilis of today as it describes in detail all that is known of salvarsan to date. The author describes salvarsan physically and to some extent chemically, explains its injection, estimates its potency, and impartially states its limitations, and demonstrates its advantages by reporting actual cases in point.

He enumerates the toxic symptoms sometimes experienced and believes that generally they are due to faulty technique in the administration and to failure to properly diagnosticate contraindications for its use in the patient; which, however, he claims are very few in number.

Fatal cases are ascribed to faulty technique and to the failure to lay the blame where it belongs, as a rule, namely in the disease. Contraindications are disposed of in four pages as being composed of serious visceral diseases.

In discussing the methods of administration the author gives precedence to the intravenous and advises repeated doses, given in pure *freshly* distilled water at body temperature.

The question of the Wassermann reaction and how it is influenced by salvarsan, is discussed in detail and examples are given

showing the reaction between the two under various conditions of medication and stages of the disease.

The treatment is applied in syphilis in all its stages and severities and conclusions drawn from actual reported cases treated by the author. The conclusions, based on facts and not theories, are as follows: (1) Salvarsan kills the spirochetes in the chancre, mucous patch, and condylomas. (2) in the secondary stage, repeated injections of salvarsan will give a negative Wassermann; (3) in the tertiary stage a negative Wassermann is obtainable and lesions clear up. But a negative Wassermann is not always to be desired here.

The drug is also useful in some of the other diseases due to protozoa and conditions like scurvy, malaria, psoriasis, etc.

If patients with lesions of vital organs or non-syphilitic nervous lesions are excluded; if only half doses be given in syphilitic nervous disease, and if patients be examined thoroughly beforehand, no fear need be entertained about using salvarsan, provided, the water used is freshly distilled the second time. E. L. E.

THE MECHANISTIC CONCEPTION OF LIFE: BIOLOGICAL ESSAYS. By JACQUES LOEB, M.D., Ph.D., Sc.D., Member of the Rockefeller Institute for Medical Research. Pp. 232; illustrated. Chicago: The University of Chicago Press, 1912.

A SERIES of ten essays, which as the title of the book indicates, have as their general tendency an attempt to analyze life from a purely physicochemical viewpoint. The subjects presented are the significance of tropisms for psychology, comparative physiology of the central nervous system, pattern adaptation of fishes and the mechanism of vision, physiologic morphology, process of fertilization, artificial parthenogenesis, prevention of the death of the egg through the act of fertilization, role of salts in the preservation of life, and the influence of environment. It is impossible for the reviewer, because of lack of training in this phase of biology, and therefore of lack of power of interpretation, to present the general biologic argument of these essays. One or two conclusions may, however, be summarized for the benefit of a medical audience.

In the opinion of Dr. Loeb, if life phenomena can be explained in physicochemical terms, "our social and ethical life will have to be put on a scientific basis, and our rules of conduct must be brought into harmony with the results of scientific biology." This it may be remembered is the argument presented by the late Christian A. Herter in his "Biological Aspects of Human Problems."

The chapter on "The Significance of Tropisms for Psychology"

closes with the suggestion that "under the influence of certain ideas, chemical changes, for example, internal secretions within the body, are produced which increase the sensitiveness to certain stimuli to such an unusual degree that such people become slaves to certain stimuli just as the copepods become slaves to the light when carbon dioxide is added to the water." Pawlow's work on the stimulation of saliva in the dog by acoustic and optic signals is quoted (Cannon's work on the influence of the emotions on the secretion of adrenalin is in accord with this), and leads the author to the observation that "it no longer seems strange to us that what the philosopher terms an 'idea' is a process which can cause chemical changes in the body."

The treatment of the various subjects presented is avowedly popular, and although the experimental material consists of the lower forms of life, the facts brought out and their discussion will prove of great interest to those interested in the underlying biologic aspects of medicine. R. M. P.

ACROMEGALY: A PERSONAL EXPERIENCE. By LEONARD PORTAL MARCK, M.D., late President of the West London Medico-Chirurgical Society and Pathological Draughtsman to St. Bartholomew's Hospital. Pp. 60; 9 plates. London: Baillière, Tindal & Cox, 1912.

THIS book being the personal record of a man afflicted with acromegaly, possesses additional value, inasmuch as the subject is a physician who has recorded very minutely and most accurately his state. Although acromegaly may be present many years before a patient consults a physician for relief from some troublesome symptom, the gross change in appearance apparently having escaped attention, it is most strange that the author, a physician, did not perceive the change in himself, for he writes: "For some fifteen or twenty years, each day when I looked into the glass to brush my hair or to shave, there was a typical acromegalic literally staring me in the face; yet I never recognized the fact." And he adds: "One might say it was a case of a secret de Polichinelle. Many of my friends, medical and non-medical, knew that I was suffering from this peculiar and rare malady; they spoke about it among themselves; some of them even thought I knew it; but none of them broached the subject to me. The strange thing was that in my case the only one not in the secret was poor Polichinelle himself, with his heavy jowl, his pot belly, his big hands and feet. It is a remarkable example of how what is obvious may be overlooked."

Poor Polichinelle, indeed, but brave. Acts of heroism, deeds

of courage, sending the blood tingling through the arteries of every man are done daily and receive their mete of acclamation. They are done in the open, before an admiring crowd, in the presence of witnesses, on the impulse of the moment, before caution with her unobtrusive voice has time to be heard. Cheers of approval and the flashing of the news across the country are hand in hand with the deed of nerve and reward it. But do these public acts of heroism constitute all bravery? The physician who suffers with an incurable disease which must not be disclosed on account of the effect on his patients, who modulates the discord of a grown seeking his lips into the harmony of a laugh which hides the clang of joylessness, who struggles on day by day against increasing weakness, pain, and distress of mind and body, dedicating himself to the good of those to whom he swore allegiance when he became their servant, with ever the knowledge gleaned from experience mocking him with its malignant certainty that his illness must have a fatal termination in about such and such a time. Is this man any less a hero than he who performs the sensational but no whit braver act? The reviewer is reminded of the condemned murderer in the "Ballad of Reading Gaol:"

"But I never saw a man who looked
So wistfully at the day
I never saw a man who looked
With such a wistful eye
Upon that little tent of blue
Which prisoners call the sky."

Dr. Mark has achieved a really great thing in thus recording amidst the tortures of what he calls the "acromegalic state" his subjective and objective symptoms. With an impersonal viewpoint which is at times uncanny in the close analysis of his case he pens well and fluently his tragic state. There is no appeal to commiseration. There is no call for sympathy. He describes in cold language cold facts, as a physician might report a "case" but we, who read between the lines,

"With sad unhelpful tears and with dimmed eyes
Look after him and cannot do him good."

E. H. G.

PELLAGRA. By STEWART R. ROBERTS, S.M., M.D., Associate Professor of the Principles and Practice of Medicine, Atlanta College of Physicians and Surgeons, Atlanta, Ga. Pp. 272; 89 illustrations. St. Louis: C. V. Mosby Company, 1912.

IN this able treatise, Roberts has assembled the data which have accumulated thus far concerning pellagra, and given them a searching and discriminating consideration. His work comprises

an interesting study of the disease in this country particularly in comparison with its manifestations in Southern Europe and Egypt. As the author states, the book is not "devoted to upholding any special theory of etiology." The arrangement of material is orderly, and the style often impressive. Of particular interest are the chapters dealing with the general characteristics of pellagra, its geographical distribution, the history of its progress in Spain, Italy, France, Egypt, and America. Most significant, naturally, is the last chapter treating of the cause of this disease. Here are arraigned against each other in complete fashion the evidence for the corn theory, and for the infective theory. Roberts, while not championing either side, presents so many more arguments for the latter than for the former that the weight of evidence appears to favor Sambon, who considers the simulium fly as the carrier of a causative organism. The discussion, however, is impartial. As the author remarks, "The advocates of corn have had a hundred years and have not made out their case. Sambon's theory is but two years old, and is being investigated."

The recognition of the various manifestations of pellagra has been described with minute care, sometimes almost at the risk of repetition, with the end result, however, that the reader obtains a clear concept of the acute attacks, the subchronic, and chronic forms, and the periods of intermission. The pathological findings in the alimentary tract, skin, and nervous system are reviewed at length, as are also the abnormal features in the other systems of the body. Some emphasis is laid on the occurrence of lymphocytosis and an increased cell count (average 35) in the cerebrospinal fluid. Treatment is satisfactorily considered. There are abundant illustrations throughout, for the most part very illuminating to the text. These include a number of maps and diagrams showing the distribution of the disease and some admirable photographs of pathological sections from the nervous system. Roberts' work is one of the few that have appeared in English on this important topic, and should command the attention of students and practitioners. One assumes that it is a printer's error which causes on page 44 the astonishing information that "maladie des saintes mains," signifying in English, "the sickness of the main saints."

H. G. S.

A Text-book of Gynecology. By William Sisson Gardner, M.D., Professor of Gynecology, College of Physicians and Surgeons, Baltimore. Pp. 271; 138 illustrations. New York and London: D. Appleton & Co., 1912.

This book has been prepared to meet the demands of the medical student. With this aim in view, the author has confined himself

strictly to the fundamentals of gynecology; facts are stated as such without modification and with only sufficient elaboration to insure a thorough understanding of the subject. While the rarer diseases are passed by with only a few words, those which the student should master are clearly detailed from the standpoints of pathology, symptomatology, diagnosis, and treatment; the anatomy of each organ likewise receives its due share of description. With the exception of three short chapters on technique and post-operative complications, the arrangement and presentation of the text closely follows that of similar text-books; in no way has the author shown originality in presenting his subject so as to more deeply impress his ideas upon the student's mind. The illustrations consist of schematic sketches, photomicrographs, and photographs of gross specimens; herein lies the weak part of the book, for in many instances the pictures convey no idea whatever of the actual condition, and even the best of the illustrations might be vastly improved upon. With this exception the book deserves commendation; it briefly but clearly summarizes the principles of gynecology.

F. E. K.

Retinoscopy (or Shadow Test) in the Determination of Refraction at One Meter Distance, with the Plane Mirror. By James Thorington, A.M., M.D., Professor of Diseases of the Eye in the Philadelphia Polyclinic and College for Graduates in Medicine; Ophthalmic Surgeon to the Presbyterian Hospital, etc. Sixth edition; pp. 71; 61 illustrations, 10 of which are colored. Philadelphia: P. Blakiston's Son & Co.

This little book gives a simple account of the method of using the shadow test. It is clearly written and well adapted to the wants of the average student. Stress is laid almost entirely upon the practical application and little upon theoretical considerations. The appearances in emmetropia and the various forms of ametropia are described and illustrated, and their interpretation explained. The writer recommends keeping the distance between the surgeon and patient constantly at one meter. This no doubt will do fairly well for the average case, but it misses the latest development by close approximation (one-third of a meter) with special mirror and light source. Compared with the one meter method, the latter plan is analogous to the use of the high power microscope as pointed out by Dr. Jackson whose labors have so largely contributed to make skiascopy the accurate test it is today.

T. B. S.

PROGRESS

OF

MEDICAL SCIENCE

MEDICINE

UNDER THE CHARGE OF

W. S. THAYER, M.D.,

PROFESSOR OF CLINICAL MEDICINE, JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND,

AND

ROGER S. MORRIS, M.D.,

ASSOCIATE PROFESSOR OF MEDICINE, WASHINGTON UNIVERSITY, ST. LOUIS, MISSOURI.

The Treatment of Leukemia and Pernicious Anemia with Thorium X.—J. PLESCH (*Berlin. klin. Woch.*, 1912, xlix, 930) reports a case of chronic myeloid leukemia treated with thorium X. There was a rapid decrease in the number of leukocytes from 109,000 to 8,800 five days after administration of the compound. On the fifty-third day following the injection the white cells numbered 4180. More remarkable than this was the disappearance from the blood of myelocytes, which originally constituted 30 per cent. of the leukocytes. Differential count showed 59 per cent. of polynuclear neutrophiles; 5 per cent. of eosinophiles; 19 per cent. of lymphocytes; and 15 per cent. of large mononuclears, essentially a normal leukocytic formula, except for the increase of the large mononuclears. In a patient with pernicious anemia admitted to the clinic moribund, with a red count of 340,000, thorium X was injected intravenously. The next day the red count was 1,200,000. It gradually increased to 1,640,000 on the fifth day, when a second injection was given. By the thirteenth day the count was 2,270,000. On admission practically no normal erythrocytes were present in the blood; on the thirteenth day nearly all the red cells were normal in appearance. Experiments on animals have shown that one hour after an intravenous injection 38 per cent. of the thorium X is in the bone marrow. The agent deteriorates very rapidly. It is a dangerous remedy, which must be employed with great caution.

Typhoid Fever.—NICLOAE and CONSEIL (*Annales de l'Institut Pasteur*, 1912, xxvi, 332) have attempted to make use of the serum of convalescent typhoid patients, and of recovered cases in the treatment

of the disease. They have employed the serum of patients who have had a normal temperature for five to eight days. After filtration, the serum was injected in repeated doses. The duration of the disease has not been shortened, but the general condition in certain cases has improved, the nervous symptoms in particular have cleared up. The benefit has been but slight, uncertain, and in every case not at all in proportion to the difficulties of application. The records of 5 cases are given which required 685 c.c. of serum furnished by 15 convalescents. In 4 patients salvarsan was given in 50 cm. doses, with no beneficial results. In fact, Nicolae and Conseil were impressed with the danger involved. In 2 cases injections of émétique failed to show results. In view of the theory of typhoid fever as a disease of the adrenal glands, adrenalin was employed. In 11 cases 15 to 20 drops of a 1 to 100 solution were given twice a day by mouth, in 12 subcutaneously. No manifest action was observed in the circulatory disturbances, or in the progress of the disease. The abscess of fixation, after Morsly, was used repeatedly, without demonstrable effect.

A New Technique for the Diazo Reaction of Ehrlich.—K. Feri (*Wien. klin. Woch.*, 1912, xxv, 919) describes a new method of performing the diazo reaction of Ehrlich. He employs paranitrodiazobenzol sulphate, known in commercial chemistry as azophorrot P. N. The test is performed in the following manner: A few granules of azophorrot P. N. are placed in a test tube with water (tap water may be used). The tube is inverted once or twice. Enough of the reagent is thus dissolved in the cold for use in the test. The urine is treated carefully with potassium or sodium hydrate (not with ammonia) until a slight turbidity remains. The aqueous solution of azophorrot P. N. is then added. If a bright red color appears and, after shaking, the foam is red, the reaction is positive. With an intense reaction the color is cherry red. In a large series of cases tested with this method and the original technique of Ehrlich, the results corresponded invariably. The advantages of the new method are several; there is the substitution of a dry substance for the two solutions, there is no necessity for accurate mixing of the reagents, and the technique is much simplified.

Cutaneous Allergy in Gonococcal Infections.—Irons (*Jour. Infect. Dis.*, 1912, xl, 77) notes the reactions following the subcutaneous inoculation of suspensions of killed gonococci in patients suffering from gonococcal infections. These reactions are characteristic and analogous to those seen after the injection of tuberculin and mallein in the respective diseases, local redness, swelling, and tenderness, focal intensifications, and general malaise, headache, and fever. For diagnostic purposes the author uses a "gonococci" of killed bacteria, suspended in glycerin. Inoculations were made after the method of von Pirquet with a control. In infected individuals, a papule was formed in a few hours, with surrounding hyperemia, disappearing by the third day. The reactions were classed as positive when over 5 mm. in diameter. In normal adults with the infection excluded, a papule of 1 to 2 mm. was formed. The reaction varies from day to day in the same individual. In persons recently infected the reaction is

negative, and increases gradually during the course of the disease. In the more chronic forms, such as arthritis, the degree of activity varies with the changes in the clinical course of the disease. Cutaneous reactions obtained with meningococcal and gonococcal antigens suggest a group reaction. In diagnosis, if infectious meningococcus or Micrococcus catarrhalis are excluded, a positive reaction is considered confirmatory evidence of a gonococcal infection.

Inclusions in the Neutrophilic Cells in Scarlatina.—DÖHLE recently described inclusions in the polynuclear neutrophiles in scarlet fever, which he considered diagnostic of the disease. His results were largely confirmed by Kretschmer. I. AHMED (*Berlin. klin. Woch.*, 1912, xlix, 1232) finds, however, that the inclusions, while frequent in scarlet fever, are by no means uncommon in other febrile diseases. Thus in 10 cases of pulmonary tuberculosis which were febrile, inclusions were found in the leukocytes in all; 5 of 10 afebrile cases of tuberculosis were also positive. A patient with tuberculous meningitis, whose blood was examined four hours antemortem, showed inclusions. In 6 cases of typhoid with high fever the result was positive. German measles furnished 1 positive case. In 2 cases of measles complicated with pneumonia no inclusions were observed, but in 2 severe uncomplicated cases of measles they were found to be present. In 2 patients with varicella without fever the result was negative, as it was in the blood of 9 healthy adults. It is evident from these findings that the inclusions are not specific for scarlatina. They may be found in febrile diseases generally.

A Source of Error in the Quantitative Determination of Enzymes in the Feces.—D. GERGANOFF (*Deutsch. med. Woch.*, 1912, xxxviii, 1130) points out the possibility of error in the quantitative determination of enzymes in the feces through the admixture of blood. Blood, whether it be from the stomach or intestines, may lead to considerable increase of the fecal ferments. (Gerganoff studied diastase particularly.) Especially intestinal hemorrhages, when large, produce a decided increase. But gastric hemorrhages, when hydrochloric acid is lacking, may lead to a similar result. When free hydrochloric acid is present in the stomach it may be concluded with reserve that a bloody stool rich in diastase is not due to gastric hemorrhage, but to bleeding from the duodenum or lower portions of the intestine. This point may prove useful in the diagnosis of a gastric ulcer or in its exclusion.

Actinomycosis Treated with Vaccines.—KENICULT and MIXTER (*Boston Med. and Surg. Jour.*, 1912, clxvii, 90) have treated with "vaccines" 8 cases of actinomycosis, 2 with abdominal, 2 with pulmonary, and 4 with cervicofacial lesions. The vaccine was prepared from pure culture grown in glucose agar. The week-old colonies were ground in salt solution and sterilized by heat and preserved in lysol. It was impossible to standardize the vaccine. Therefore treatment was begun with very small doses, which were generally increased in strength. In addition, all collections of pus were incised and drained. The thoracic cases were advanced when first seen. They grew rapidly

worse and died. The vaccine caused an immediate large increase of granules in the sputum, lasting several days. One of the abdominal cases, after drainage of an abscess in the groin has apparently completely recovered after two months of vaccine treatment. The second died after varying periods of improvement. The impression was that the acute process was held in check. Of the 4 jaw cases, 3 have recovered, and 1 is rapidly improving. It seemed to Kenicult and Mixter that the use of vaccines in superficial actinomycosis does do good.

The Results of the Treatment of Pulmonary Tuberculosis with Rosenbach's Tuberculin.—R. KOHLER and M. PLAUT (*Zeitsch. f. klin. Med.*, 1912, lxxiv, 179) have employed Rosenbach's tuberculin in the treatment of pulmonary tuberculosis. This preparation represents one of the many attempts which have been made to obtain a less toxic substance than Koch's old tuberculin. It is a cluture of tubercle bacilli inoculated with Trichophyton holosericum album. The latter alters (digests) proteins, and it is supposed that the toxic, labile molecules of the tubercle bacilli are attacked. The toxicity of this tuberculin is apparently about 100 times less than the old Koch's tuberculin, while the active immunizing property is undiminished in strength. Kohler and Plaut have selected 80 dispensary patients, most of whom were in the first stage, though some were in the second stage of pulmonary tuberculosis. One-half of them were treated with tuberculin, the remaining half being treated with hygienic and dietetic measures alone. The patients were carefully followed for several months. The results obtained in the group treated with Rosenbach's tuberculin were strikingly good. The disease was favorably affected in 85.4 per cent. of the cases, whereas only 36.8 per cent. of the controls improved. The result is even better than this would indicate, for the patients treated with tuberculin had not the benefit of the hygienic measures used with the controls. A gain in weight was noted in 70.2 per cent. of the patients treated with tuberculin, in 33.4 per cent. of the controls. Of the tuberculin patients, 16 had elevations of temperature when they came under treatment; in 13 the temperature became normal, in 3 it was uninfluenced. The effect of the tuberculin on the subjective symptoms of the patients was the most remarkable feature of the treatment. Many of the patients were sceptical in the beginning, and frequently complained of sore arms from the injections; it is probable that suggestion can be eliminated. Nevertheless, the cough lessened or disappeared completely; night sweats, of which the majority complained, had ceased in all but 4 cases. The appetite was greatly increased, and pains were diminished or vanished. Reactions to the tuberculin were both local and general (swelling and pain in the arm, elevation of temperature, etc.). In many instances the local signs in the lungs increased shortly after the institution of the tuberculin treatment, to improve later. The case histories are given in considerable detail, and the dosage of the tuberculin is considered.

The Gastro-intestinal Disturbances of Pernicious Anemia.—In 58 cases of pernicious anemia, FRIEDENWALD (*Boston Med. and Surg. Jour.*, 1912, clxvii, 160) has made close observations of the gastro-intestinal manifestations. Loss of appetite was observed in 38 cases,

nausea in 27, vomiting in 19, indigestion in 33, diarrhea in 20, constipation in 27. Enteroptosis was present in 21 instances, atony of the stomach in 29. In 30 cases there was absence of gastric secretion. The total acidity ranged between 8 and 14. In 9 cases analysis during a period of improvement in the blood and general health did not show a return of gastric secretion.

Trichiniasis.—The researches of ROMANOVITCH (*Annales de l'Institut Pasteur*, 1912, xxvi, 351) upon trichiniasis emphasize the advisability of daily examinations of the circulating blood after the ingestion of suspected food. The female parasite penetrates the mucous membrane of the intestine, but never deeper than the muscularis. She does not reach the mesenteric glands. The larvæ are deposited in the lymph vessels or their neighborhood, and reach the circulating blood through lymphatic channels. The larvæ can enter serous cavities, peritoneal, pleural, and pericardial, but they are destroyed rapidly. It is definitely demonstrated that the larvæ penetrate the sheath of the primitive muscle fibre. This is because here better than elsewhere, the nutritive elements are found of which it has need. In traversing the intestinal mucosa the female is accompanied by bacteria. The character of infection in the blood of man and animals infected is polymicrobic. The serum of infected rabbits becomes very toxic, as early as nine days after the ingestion. The toxicity corresponds with the intensity of the larval infestation. The animals which survive an injection of the toxic serum show great wasting. The search for antibodies is unsatisfactory, both by the method of precipitins and by complement fixation. An observed case of re-infection confirms that of other authors and emphasizes the impossibility of immunizing against a new infestation. There is no preventative or abortive treatment. Salvarsan has no effect.

Viscosity of the Blood and Its Relation to Venous Murmurs.—J. MATSUO (*Deutsch. Archiv f. klin. Med.*, 1912, cvi, 433) has examined the viscosity of the blood of a large series of healthy and anemic Japanese; at the same time hemoglobin estimates and counts of the blood cells have been made. His attention has been directed chiefly to the occurrence of anemic or hemic murmurs. He finds a *bruit de diable* almost invariably present when the viscosity is below 2.8; when the viscosity rises to 3 or 3.1 the murmur disappears. In the majority of cases the intensity of the murmur is inveresly proportional to the viscosity value.

The Effect of Meat Extractives on the Utilization of Vegetable Diet.—H. WOLFF (*Zeitsch. f. klin. Med.*, 1912, lxxvi, 66) has continued his investigations of the effect of extractives on the utilization of vegetable food. His first studies were made on dogs. The present observations were made on man. He finds (1) that persons on a vegetable diet, insufficient of itself to meet the nitrogen requirement of the body, improved greatly under the administration of 5 grams of Liebig's beef extract, the nitrogen metabolism being practically in equilibrium. The result was due partly to better utilization of the nitrogen in the food and partly to a lessened excretion of nitrogen. (2) During the

administration of the beef extract an increase of uric acid occurred in the urine. On the supposition that the nitrogen of the excess of uric acid was derived from the beef extract, then 20 per cent. of the nitrogen of the beef extract was excreted in the form of uric acid. (3) Starch was better utilized; the absorption of it increased 25 to 30 per cent. under beef extract. (4) On the fat metabolism an effect was noted in two directions: (*a*) The fat was more completely split, and (*b*) the absorption was increased. (5) A comparison of these results with those obtained on dogs suggests the conclusion that improvement of the nutrition from vegetable food follows the giving of beef extract only so long as unutilized food remains in the alimentary canal. Increasing the beef extract beyond the amount necessary to produce the desired result does not appreciably alter the metabolism.

Effect of Adrenalin, Pilocarpine, and Physostigmine on the Eosinophilic Cells.—G. SCHWENKER and H. SCHLECHT (*Zeitsch. f. klin. Med.*, 1912, lxxvi, 77) have previously noted the marked eosinophilia both in the peripheral blood and in the lungs associated with anaphylactic shock in guinea-pigs. They have attempted to determine whether stimulation of the autonomic nervous system may be the explanation of the phenomenon. Their experiments were done on dogs and guinea-pigs. As excitants they used adrenalin, pilocarpine, and physostigmine. Following adrenalin there is a marked decrease or entire disappearance of the eosinophiles from the peripheral blood. Pilocarpine and physostigmine have no effect at all, or lead to results similar to those obtained with adrenalin. They were unable to produce a local eosinophilia, such as they have observed in the lungs in anaphylactic shock, after injection of adrenalin, pilocarpine, or physostigmine. Likewise the liver, spleen, kidneys, lymph glands, and bone marrow exhibited no increase of eosinophiles. Schwenker and Schlecht concluded that stimulation of the autonomic or sympathetic nervous system is in itself insufficient to explain the eosinophilia of anaphylactic shock in the guinea-pig.

Chlorine Content of Blood Serum in Secretory Disturbances of the Stomach.—W. ARNOLD (*Zeitsch. f. klin. Med.*, 1912, lxxvi, 45) has examined the chlorine-content of the blood serum of patients with secretory disturbances of the stomach to determine the relationship, if any, between the chlorine-content of the serum and the hydrochloric content of the gastric juice. Serum was employed rather than whole blood, for it has been shown that it is relatively richer in chlorine and that the determinations can be made more accurately. He finds (1) that there is a change in the chlorine content of the serum with the onset of secretion of the gastric juice. (2) With anacidity and subacidity the serum constantly contains more chlorine than in hyperacidity, and at the same time the water-content is somewhat increased. (3) Some patients with anacidity whose condition cannot be differentiated clinically, presented a decreased chlorine-content of the blood serum. (4) A few cases with changing hydrochloric acid content were examined and they showed a relatively high per cent. of chlorine in the serum.

SURGERY

UNDER THE CHARGE OF

J. WILLIAM WHITE, M.D.,

FORMERLY JOHN RHEA BARTON PROFESSOR OF SURGERY IN THE UNIVERSITY OF PENNSYLVANIA AND SURGEON TO THE UNIVERSITY HOSPITAL,

AND

T. TURNER THOMAS, M.D.,

ASSOCIATE PROFESSOR OF APPLIED ANATOMY IN THE UNIVERSITY OF PENNSYLVANIA; SURGEON TO THE PHILADELPHIA GENERAL HOSPITAL, AND ASSISTANT SURGEON TO THE UNIVERSITY HOSPITAL.

A New Method of Gastrostomy and Esophagoplasty.—ROPKE (*Zentralbl. f. Chir.*, 1912, xxxix, 1569) says that the oblique or tortuous canal provided by the usual methods of performing a gastrostomy, sooner or later changes under tension and becomes a more or less direct fistula leading into the stomach. The feeding tube passes in and out loosely, the stomach contents escape alongside, and the surrounding skin becomes sore and inflamed. Ropke reports a case of cancer of the lower end of the esophagus in which he performed an operation devised by Jianu, who had performed it experimentally on dogs and on the human cadaver. In Ropke's case there was found a nodular tumor the size of the fist, which was inoperable. The abdomen is opened by an incision in the median line above the umbilicus. The omentum is separated along the greater curvature, the gastric arteries and veins being carefully avoided to the neighborhood of the pylorus, where they are double ligatured and divided. From the pylorus a quilted suture is introduced through both walls of the stomach up to the fundus. The suture ends just above where the left gastric artery reaches the stomach and includes between it and the greater curvature, a narrow strip of stomach about $2\frac{1}{2}$ fingers' breadths wide. This strip is left to communicate with the rest of the stomach at the cardiac end, but is cut off from the stomach in the rest of its extent by the suture. Beginning at the pyloric end this narrow strip of stomach is divided from the rest from the pyloric end up to its cardiac end, where it remains attached and is turned outward and wrapped in gauze. The quilted suture is then turned in and covered by a sero-muscular suture in its whole extent and the latter suture is continued to the cut edges of the separated flap, so that from it is made a tube leading into the stomach. The peritoneal cavity is then closed around the attachment of the new tube to the stomach where the stomach is fixed in the abdominal wound without disturbing the sutures of the new tube. The latter is now completed, a small tampon is inserted into its end and fixed by a suture, and the end of the canal is turned in over the tampon by a suture. According to the length of the new canal—in Ropke's case 22 cm.—a tunnel is made of varying length upward, under or through the pectoral muscle from the abdominal wound toward the left clavicle. With a long forceps the new stomach canal

is drawn through this tunnel. The abdominal wound is then closed completely. The upper end of the gastric canal is sutured closely to the edges of the upper end of the tunnel, its closing suture is removed, the small tampon in its end is taken out, and the edges of its mucous membrane are sutured to the skin edges of the surrounding wound. Good healing occurred. After eight days fluid and pulpy food were passed through the new canal into the stomach, and this was kept up afterward. No backflow of stomach contents occurred.

The Necessity of Suturing Incisions of the Pelvis and Ureter.—Bazy and Bazy (*Jour. d'Urolog.*, 1912, ii, 645) consider that one should not follow a uniform course in the matter of suturing the pelvis and ureter after incision into them. They do not agree with those who say that the suture ought always to be employed, any more than with those who believe that it ought never to be used. They believe that its use should depend upon the possibility or facility with which it can be employed. They are convinced that it is an excellent practice and that the results which it gives are constantly good. But as it is not absolutely necessary, it should not be attempted at the risk of compromising the success of the operation. One should avoid with care denuding the urinary ducts and separating them from the cellulo-adipose tissue surrounding them, which fortify and carry nourishing vessels to them. It is upon these tissues, rendered resistant by the irritation from the presence of the calculi, and upon them alone that one will depend to hold the suture. Under these circumstances it can be introduced easily, rapidly, and efficaciously, and it will not be followed by contractures. When the pelvis and ureter have been denuded, suture is often impossible and in such cases it will be well to cover the opening and protect the duct by a plastic flap made from the surrounding tissues. Suture should not be employed when it appears to be difficult and in consequence gives little chance of a satisfactory result, nor when it appears to be dangerous from the standpoint of the ulterior integrity of the calibre of the urinary tract. It should not be done in patients with a precarious general condition, or when after a laborious operation it seems especially important to shorten the duration of the operation. A septic condition of the urine is not a contraindication to the suture. Nevertheless, when the infection appears to be serious and a ureterotomy has been done, it will be best, in place of attempting removal of the margins, to provide drainage of the ureter, which seems to have very desirable advantages.

Cutaneous Autoplasty in the Cure of Grave Urethro-rectal Fistulæ.—Michon (*Jour. d'Urolog*, 1912, ii, 681) says that some urethro-rectal fistulæ are particularly grave because of the extent of the destruction of the posterior urethra and the cicatricial induration of the perineal tissues, and demand other than the ordinary procedures for their cure. Michon obtained a good result in such a case with the following operation: A small cutaneous flap is cut from the posterior median part of the scrotum, rectangular in shape, 3 cm. long, and wide enough so that with its anterior end attached to the scrotum, it can be drawn without difficulty into the perineum. It is at first left attached by its two small ends, the one anterior and the other posterior,

and the underlying scrotal wound is closed by sutures. At the end of five or six days the posterior pedicle is divided, thus giving a movable flap attached to the scrotum with good vitality. A preanal incision is made transversely and the rectum detached up to the prostate exposing both fistulous orifices. The flap is then drawn into the wound, its cutaneous surface being turned anterior and its raw surface posterior, the posterior extremity being immediately below the loss of substance in the urethra. It is then fixed in this position by catgut sutures to the urethra and lateral tissues. The adhesion is to take place only in the depth of the wound and not along the whole anterior wall. To prevent this a little rubber tissue is interposed. The wound is tamponed carefully each day to favor the attachment of the flap in its new position. When this has been accomplished, which requires at least two weeks, one begins to divide the scrotal pedicle. This is done very slowly, at intervals of several days, and one should not forget that the perineal tissues are sclerotic and that the new vessels form very slowly. Finally when the flap is divided, its upper end is adherent to the urethral orifice only. For several days the flap is pressed into the depth of the wound by the dressings toward the position it is ultimately to occupy. The perineal wound is again opened and deepened until the posterior surface of the prostate is well exposed and the inferior free end of the flap is pushed upward turning the flap on its attached end as on a hinge. It is then fixed by sutures to the posterior surface of the prostate. The perineal wound is closed except for a small drain.

Circular Resection and Suture of the Axillary Artery for Transverse Laceration by Fracture dislocation of Anatomical Neck of the Humerus.—BUCHANAN (*Surg., Gynec. and Obst.*, 1912, xv, 648) removed a segment of the artery at the site of the laceration and reëstablished its continuity by circular suture. The patient made a good recovery but has never had a distinct radial pulse and up to the time of writing has considerable spasticity and some limitation of motion at the shoulder. The small number of cases of circular arterial suture reported to this date can be accounted for in a variety of ways: as by the fear of consequitive or secondary hemorrhage; the expectation of weakening of the vessel with resultant aneurism; the idea that the operation is difficult and requires special skill or previous animal experimentation and special instruments; the belief that thrombosis is to be expected, which will put the procedure on a par with ligation; the opinion that atheroma contraindicates arterial suture; the fact that ligation, in a very large proportion of cases, is followed by development of the collateral circulation and a result equal to arterial suture. Taking up these points in detail, the following facts should be considered (1) Hemorrhage has never followed circular suture, and in but one of the reported cases of lateral suture. This is probably due to the reason that where perfect primary union is not secured by the accurate suture, thrombosis will promptly occur, which will sufficiently plug the vessel before the stitches could possibly give way. (2) Aneurysmal dilatation has never been observed after arterial suture. (3) The operation on vessels of the size of the femoral or axillary is no more difficult than many others that the general surgeon daily performs.

Animal experimentation to acquire dexterity is certainly desirable but not essential to success for the ordinary operator. Instruments required are only such as are present in every well-equipped operating room. Thrombosis undoubtedly occurs after many arterial sutures, but in the interim the sutured vessel remains patulous and performs its function until its gradual closure by a thrombosis has induced dilatation of the collateral vesssels. The writer's case is but one among a number which shows that no harm may result from arteriorrhaphy in vessels markedly atheromatous. Gangrene occurs in a certain proportion of cases of ligature of main arterial trunks (stated by Wolf as 15 per cent. in the cases of axillary ligation) and certainly some of these unfortunate results can be saved by circular suture.

Results of Experiments on Kidneys with Special Reference to Decapsulation and Establishment of Collateral Circulation.—SITER (*Surg., Gynec. and Obst.*, 1912, xv, 702) did a series of experiments on cats and dogs, in which he first decapsulated one kidney and wrapped it in omentum. At a later period the abdomen was opened and the artery to this kidney tied off. Still later the animal was killed and the resulting conditions were studied. The following facts were established: The kidney increased in size upon decapsulation. The wrapping of the kidney in the omentum is immediately successful in forming a new capsule. The collateral circulation is established at the end of ten days. The collateral circulation is sufficient to allow the kidney to functuate properly when the renal vessels are tied off. The kidney remains much enlarged when the capsule is removed. The forming of a new capsule from the omentum prevents adhesions between the kidney and the surrounding soft parts and increases the blood supply.

Appendicular Hernia and Hernial Appendicitis.—NORRLIN (*Arch. gén. de chir.*, 1912, vi, 1303) reports 2 cases of inflamed and strangulated appendix found in the sac of a femoral hernia. According to Glogg and others, nearly 2 per cent. of all hernias have the appendix as a part of the hernial contents. In the 2 cases here reported only the appendix was found in the sac, and it is to this particular form of the condition that attention is directed. Of 21 such cases of femoral hernia reported by Honsell, 19 were in women, aged over forty years. Of 53 analogous cases reported by Glogg, 50 were in women and on the right side, and the 2 here reported were in women, aged sixty-one and seventy-one years. The strangulation of the appendicitis can be the initial lesion. All authors agree that the diagnosis of the appendix isolated in a hernial sac is very difficult. Kirmisson made the diagnosis in one case, but there were no symptoms of intestinal occlusion. Symptoms of intestinal occlusion may be absent also when Meckel's diverticulum is strangulated, in a Littre's hernia, or in the strangulation of an epiploic appendage. In operating one ought to open the abdomen at another place in order to clear up the facts and to permit a proper estimation of the condition of the lesion. Since the peritoneal cavity is opened in a hernia operation it would be an easy matter to find and remove the appendix which would be particularly advisable if it is the seat of a chronic inflammation or a foreign body. Fortunately most inguinal and femoral hernias are on the right side.

The Mechanism of Chronic Retention in Prostatics.—VIRGHI (*Jour. d'Urolog.*, 1912, ii, 823) says that this subject has properly received much attention in recent years from urologists because in the solution of the complex problem involved lies the explanation of the urinary troubles associated with hypertrophy of the prostate. All causes of a transient or inconstant character, such as reflex inhibition, median lobe, valves of the neck, etc., should be discarded from the general discusion of the mechanism of retention. They are incapable of producing phenomena of a permanent or chronic character. Diminution or disappearance of the contractility of the muscular system of the bladder does not account for the retention in hypertrophied prostate, because micturition returns to the normal after the complete removal of the prostate, which shows that the detrusor muscle never lost its functional value, since this returns as soon as the obstacle has disappeared. The prostatic obstacle can contribute to but not create the retention. The retention is due to lesions of the sphincter of the neck, causing disturbances of the function of the sphincter during micturition and an incomplete evacuation of the bladder. Retention does not occur if, notwithstanding hyperplasia of the gland, the muscular structure of the sphincter of the neck does not undergo histological alterations. The suppression of the retention and the return of spontaneous micturition, after operations on the prostate, are due to the removal of the cervical sphincter by the operation. If one destroys the sphincter of the neck alone in an hypertrophied prostate by a special operation, he can avoid the performance of a total prostatectomy in a number of cases, and at the same time cause the disappearance of the retention. Retention in false prostatics is due to lesions of the sphincter of the neck and not to a reflex inhibition.

A Contribution to the Study of Urethritis.—ROUCAYROL and RENAUD-BADET (*Jour. d'Urolog.*, 1912, ii, 835) reports with much detail a case which he summarizes as an old chronic urethritis reawakened by an attack of grippe, with the development later of an intrabicipital abscess which was incised, and in which was found the gonococcus, modified in its form and reactions. Gonococcic vaccine was given and a cure obtained. The case shows that an old chronic urethritis can conceal the gonococcus in a condition of retarded life, while bacteria examinations of the urethral discharge show no trace of it. These gonococci with retarded life are susceptible, under the influence of unknown causes, of reawakening and producing complications in different parts of the body. The cause of the re-awakening in this case was the grippal infection, the microbic association of which gave a new virulence to the gonococci, which had been torpid and well tolerated up to that time. The case shows also that auto-intoxication can play an important part in the treatment of gonococcic infection. A local treatment may be too intensive. In deep lesions the treatment should act mechanically to provoke by irritation absorption of the microscopic elements, while the microbes are being attracted toward the surface of the lesions. If a new microbe makes its appearance in full activity, by virtue of the law of microbic associations, the gonococcus takes on new virulence, and may be capable of grave consequences. The extragenital localization of the infection appears to be

a means of defence, and the bicipital abscess in the case here reported, seemed to be an example of this kind. The results obtained with the gonococcic vaccine are much superior to those obtained with the ordinary therapy in vogue. Local treatment is effective locally in a case of gonococcic septicemia, but it does not affect the microbes and toxins in the blood. The salts of silver introduced into the circulation furnish appreciable results, but they are not specific. The vaccine, on the contrary, especially the autogenous vaccine prepared by culture of the blood, causes with the least reaction a progressive and definite immunity against the infectious agent. It is a vigorous specific. In this case the microbe found was analogous in all points but was not the typical gonococcus.

THERAPEUTICS

UNDER THE CHARGE OF

SAMUEL W. LAMBERT, M.D.,

PROFESSOR OF APPLIED THERAPEUTICS IN THE COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, NEW YORK.

The Treatment of Articular Rheumatism with Atophan.—BENDIX (*Therapie d. Gegenwart*, 1912, liii, 301) gave atophan in doses of from 1 to 5 grams per day to 100 cases of articular rheumatism, with very good therapeutic results. The length of treatment varied from ten days to a period of several weeks. He gives a tabulated report of all the cases treated, dividing them into groups as to results obtained by the treatment. Of the 100 cases, 45 were rapidly cured. These 45 were especially acute cases with high fever and marked joint involvement. The temperature became normal in most of these patients after two or three days of treatment, and the joint manifestations disappeared a few days later. The second group comprised the cases denoted as improved, and of these there were 28. Most of these patients had very little evidence of rheumatism after the treatment, except joint pains and stiffnes :hat recurred after discontinuance of the remedy. The third group of 27 cases was not influenced by the treatment. More than half of this group were complicated by other diseases. The rheumatism was also of more than two weeks duration, and a few salicylic acid preparations had given no relief. Bendix says his experience with atophan in articular rheumatism leads him to the conclusion that its action is extraordinarily similar to that of the salicylic acid preparations, and only slightly inferior to them. The explanation of its action can be determined only by further experimentation. Atophan is free from untoward effects even when given in large doses over long periods of time. Three grams a day are sufficient given in divided doses, and it should be administered for at least six successive days in this way unless results are obtained within

that time. In most cases which resist salicylates, atophan will give relief if not a complete cure. He recommends, therefore, the use of atophan especially for such cases.

Antityphoid Inoculation for Nurses.—SPOONER (*Jour. Amer. Med. Assoc.*, 1912, lix, 1359) has instituted antityphoid inoculation in various training schools for nurses in Massachusetts during a period of three years, and in his article relates his observations on the subject. He says that frequent injections of small amounts of a low-virulence cause slight inconvenience. They seem to produce a protection among nurses, who are eight times more liable to the disease than the average individual. Their morbidity, under ordinary conditions, is 1.4 per cent., or 19 cases among 1361. Only 2 cases developed under these conditions. Case morbidity among the uninoculated in these hospitals is nearly nine times greater than among the inoculated, subjected to similar conditions. No permanent untoward effects have arisen from over 5000 injections. The blood picture indicates a certain protection lasting at least two and one-half years. The use of this means of protection has been shown to be safe in two epidemics, and very efficient in at least one of them.

Curative and Prophylactic Inoculation for Human Tuberculosis.—FRIEDMANN (*Berlin. klin. Woch.*, 1912, xlix, 2214) writes concerning his method of treating tuberculosis. He does not give the details of the method of preparation of his material for inoculation, but indicates that it is prepared from a variety of the tubercle bacillus which was naturally free from nearly all toxic action, and which was only slightly virulent for man. Friedmann has applied his method of treatment to 1182 cases of tuberculosis of all kinds in various clinics and hospitals under the constant critical observation of many physicians. The remedy had no untoward results even when given in larger doses than necessary for therapeutic effects. He reports uniform improvement and cures in practically all the cases treated, although his statements as to the results are general, and no exact details are given. After the treatment was shown to be harmless, children constantly exposed to tuberculosis were given prophylactic injections of the remedy. A single intramuscular injection was thus given to 335 children aged from one hour to three years. All of these children have borne the inoculation, which was given over a year ago, without the least harm. These children were, at the time of this report, free from any indication of "scrofula" or tuberculosis. Guinea-pigs were injected with very large doses of the remedy without their showing any untoward effects from the inoculation. When killed years later they were found to be entirely healthy. The avirulent bacilli had been entirely absorbed, and Friedmann believes that a certain degree of immunity was produced by the injections. The animals thus immunized were able to resist severe artificial infection; the immunized animals survived on an average, 363 days, while 10 untreated controls lived only 110 days. However, all the injected animals died eventually of the tuberculosis produced by the artificial injection. Friedmann believes that the conditions of infection in man are never so menacing as in artificial laboratory infection, and he thinks his method of treat-

ment will produce permanent protection against human tuberculosis as ordinarily contracted. In the discussion by physicians who had observed Friedmann's cases, a number confirmed his statements regarding the results obtained, but others were not so favorably inclined to the remedy. Citron and Klemperer spoke against the principle of the treatment, as they thought that the use of avirulent bacilli is dangerous since they are liable at any time to become virulent. They cite Pasteur's experience with the use of an avirulent vaccine for the treatment of chicken cholera that subsequently became very virulent. The prophylactic effect of a single injection of the remedy to infants as a prophylactic measure was questioned on the ground that it could be of little benefit to infants in later life, because any prophylactic effect would only be active as long as the bacilli remain alive within the body. A number of other objections were made against accepting the remedy until more was known as to its composition.

The Treatment of Human Cancer with Intravenous Injections of Colloidal Copper.—Loeb, McClurg, and Sweek (*Interstate Med. Jour.*, 1912, xix, 1015) give a preliminary report as to their results with intravenous injections of colloidal copper in the treatment of human cancer. They used a colloidal solution of copper prepared according to Bredig's method. Each patient received daily an intravenous injection of 300 to 400 c.c. of the solution, warmed to about body temperature. The injection was invariably followed by a rise of temperature, and frequently accompanied by a more or less severe chill. This reaction became less marked after several injections. The patients bore the injections well; their general condition improved, and pain was so much relieved that anodynes were no longer necessary. With regard to the effect upon the tumor, they say that about two to four hours after the injection hyperemia is noticeable in the tissue adjoining the tumor. This hyperemia is often accompanied by an increase of discharge from ulcerating tumors, and by an increased sensitiveness of the tumor. Hyperemia and sensitiveness gradually disappear after about fifteen injections, and a gradual necrosis and resorption of the tumor occurs. So far the retrogression has been continuous, and at least 2 cases are near a complete cure. They report 8 cases; 2 of these had internal metastases and terminated fatally. The other 6 were cases of inoperable cancer of the face, jaw, neck, and cervical glands. Most of these had been operated upon before without success. In all of these the copper injections caused a marked retrogression of the tumor. They do not express any definite opinion on the ultimate results of this method, but hope that further investigations will lead to a still wider extension of the applicability of this mode of treatment.

Administration of Antitoxin.—Park (*Boston Med. and Surg. Jour.*, 1912, clxviii, 73) says that the dose of diphtheria antitoxin advised by the health department of New York City for purposes of immunization is 1000 units. This dose should be repeated in ten days if danger of infection still exists. The use of tetanus antitoxin as a preventive measure has given very good results. The initial dose of

tetanus antitoxin for immunization is 1500 units and this should be repeated in fifteen days if necessary. Park emphasizes the importance of giving the required amount of antitoxin promptly, and in a single dose. He says that when diphtheria antitoxin is given subcutaneously it is present in the body fluids in a small amount on the first day, but the amount of antitoxin increases and reaches its maximum on the third and fourth day after the administration. With regard to the weight of the patient as a factor in influencing the size of the dose, Park believes that there is no question that the concentration of antitoxin in the blood and not the total amount measures the effect. He urges the intravenous method of administering diphtheria antitoxin in severe cases of diphtheria. The difference during the first day in the amount of antitoxin in the blood when injected intravenously and when injected subcutaneously is very great. At the end of six hours one has, with a proper dose by the subcutaneous method, 2 units, and by the intravenous method, 20 units in each cubic centimeter of blood. As the hours pass one diminishes and the other increases, but even at the end of twenty-four hours, there are 12 units if the antitoxin is administered intravenously against 6 units if given subcutaneously. Park says he feels sure that 5000 units given intravenously has as much effect as 20,000 given subcutaneously. He has seen intravenous injections of refined antitoxin given in nearly 200 cases, with no bad effects. It is necessary to cut down on the vein in little children, but with adults and larger children this is unnecessary. Park thinks that all cases of septic diphtheria should be given the antitoxin intravenously; but in mild and early cases it is sufficient to give it subcutaneously. Intramuscular injections are absorbed in about one-half the time required by subcutaneous ones, when the serum stays in the muscle substance; but, in practice it often escapes. Park says he has often seen life saved in tetanus by intravenous injections of tetanus antitoxin. He advises the intravenous injection of 20,000 units at the very first indication of tetanus without waiting to be certain of the diagnosis. In cases where the rigidity continues after this initial dose, the injections of smaller amounts should be repeated at twelve-hour intervals for several days, although he is doubtful as to the value of repeating the injections.

Changes in the Liver after the Administration of Salvarsan.—Severin and Heinrichsdorff (*Zeitschr. f. klin. Med.*, 1912, lxxvi, 138) report 2 cases in detail that gave marked clinical evidence of liver disease simulating acute atrophy before death and at the autopsy showing evidences of marked degenerative changes in the liver. Both of these patients had received salvarsan for luetic infections, and the question was raised whether the liver changes were induced by arsenic or were the results of syphilis. They came to the conclusion that the degenerative changes in the liver in one case were due to the arsenic, and in the other were probably due to endotoxins derived from the spirochetæ pallida. Severin and Heinrichsdorff say that these liver changes should only be ascribed to salvarsan upon the following conditions: (1) The clinical symptoms must follow the administration of the salvarsan. (2) There must be a definite relationship between the apparent age of the lesions produced by the salvarsan and the period

of time elapsed since the administration of the remedy. (3) The more recent areas of degeneration in the liver must contain arsenic. These three conditions were fulfilled in one of the cases reported, and were lacking in the other fatal case in which syphilis could not be excluded as the cause of death.

Absorption of Arsenic Following Intramuscular Injections of Salvarsan and Neosalvarsan.—SWIFT (*Jour. Exper. Med.*, 1913, xvii, 83) says that intramuscular injection of salvarsan and neosalvarsan in rabbits always produces necrosis of the muscles. A much more intense reaction is produced by salvarsan than by neosalvarsan. The rate of absorption of arsenic following intramuscular injections of salvarsan is very slow, while following intramuscular injections of neosalvarsan between 75 and 85 per cent. of the arsenic is absorbed during the first week. The subsequent absorption is quite slow. The rate of absorption was most constant after the injection of the neutral suspensions, a little more irregular after the injection of the alkaline solution, and most irregular after the injection of the acid suspensions. This is what might be expected if the rate of absorption is dependant upon the degree of injury produced by the injection, since neutral solutions inflict the least injury. During the first week after intramuscular injections of neosalvarsan as much arsenic was absorbed as after six weeks of salvarsan. After the first week the small amount of arsenic remaining in the muscles after neosalvarsan injections was slowly absorbed, and only about 5 per cent. remained at the end of six weeks. Swift says that the solubility of neosalvarsan combined with the neutral reaction of its solution probably explains its superiority over the old form for intramuscular injections.

Benzol in the Treatment of Leukemia.—STEIN (*Wien. klin. Woch.*, 1912, xxv, 1938) reports a case of myelogenous leukemia treated with benzol, with very great benefit. This patient had been treated systematically by the Röntgen rays, and was only slightly benefited by it. The patient was a woman, aged sixty-seven years, whose leukocytes were 225,000 when the benzol treatment was begun. As a result of the treatment, according to Stein, the leukocytes fell to 6000 and the morphology of the white cells approached more nearly that of normal blood, although a differential count still showed a small percentage of myelocytes. At the same time a marked improvement in the general condition occurred, including an increase of weight and a disappearance of all the subjective symptoms. The spleen which extended below the level of the umbilicus and to the median line before the treatment, was no longer palpable when the treatment was discontinued. The benzol was given in enteric capsules for a period of six weeks, and at the end of this time the patient was given small doses of arsenic. The marked improvement as noted above occurred while the patient was on benzol alone.

Untoward By-effects with Neosalvarsan.—SIMON (*Münch. med. Woch.*, 1912, lix, 43) reports 2 cases that developed severe toxic symptoms after the administration of neosalvarsan. These symptoms were a rash, collapse, unconsciousness for several hours, and violent

headache after recovery of consciousness. Simon denotes these as angioneurotic symptoms, due to congestion or acute swelling of the brain. These severe untoward effects may be ascribed to too high dosage, considerably higher than that of salvarsan. If given in doses equivalent to those of salvarsan, no such untoward results were obtained.

PEDIATRICS

UNDER THE CHARGE OF

LOUIS STARR, M.D., AND THOMPSON S. WESTCOTT, M.D.,

OF PHILADELPHIA.

Creosotal in Pediatrics.—GEORGE HUNNAEUS (*Medizin. Klinik*, 1912, viii, 1586) gives his conclusions on creosotal based on 150 cases treated with this drug. Creosotal is not unpleasant to the taste and can be given to children very easily in warm milk. It is quickly absorbed, and creosote is found on the breath and in the urine in one hour after creosotal is ingested. It imparts to the urine an olive-green tint which has no harmful significance. Creosote also appears in the bowel and is absorbed there. Creosotal has been used particularly in France in very large doses in pneumonia, with excellent results. It tends to reduce the fever but must be exhibited until the lungs are entirely clear, to avoid a reinfection. Toxic symptoms, as delirium and convulsions, usually disappear within twenty-four hours under creosotal. Broncho-pneumonia complicating measles is favorably influenced by creosotal, and Hunnaeus gives it as a prophylactic on the appearance of Koplik's spots. It is especially beneficial in chronic bronchitis, in which it improves the appetite and general strength besides its good effect locally on the lung condition. Creosotal must be given in relatively large doses, even in infants. Hunnaeus gives the following table of doses, giving the drug three times a day: Up to one year, 5 drops; two years, 10 drops; three to four years, 15 drops; five to six years, 20 drops; seven to ten years, 25 to 30 drops. The original package of creosotal by "Heyden" or "Bayer" contain the best and purest preparation. In many cases of pneumonia the drug acts almost as a specific. It is also of considerable value in pulmonary tuberculosis in children.

The Etiology of Convulsions in Early Life.—FLOYD M. CRANDALL (*Archives of Pediatrics*, 1912, xxiv, 803) brings to notice the fact that prevention of convulsions in children is vitally important, since attacks of this nature several times repeated may lead to epilepsy in later life through the formation of an insidious inclination or even habit on the part of the brain to such discharges of energy. A large number of adult epilepsies begin really in childhood and as early as the first year. Prophylaxis is therefore very important and depends on a knowledge of the etiology of the condition in any one case. In-

fancy and childhood are themselves predisposing factors on account of the disproportionate growth of the brain during this period of life, while the control of the higher centres is slight. Heredity is another predisposing cause of convulsions. This is frequently seen in certain families in which it can be traced for several generations. Tendency to convulsive disorders is often an early symptom of rachitis, an etiological factor which should always be looked for. Among the exciting causes of convulsions are the two main groups, organic and reflex. Meningitis, tumors, and hemorrhage of the brain, etc., belong to the first group. Under the second heading dentition and phimosis, while undoubtedly causing a disturbance are rarely alone the cause of convulsions. Undigested food masses in the intestinal canal, coupled with toxemia, is the most common reflex cause of convulsions. Toxic causes include uremia and the infectious diseases, especially pneumonia and pertussis. Every seizure demands a close study to determine the underlying causes, so that further attacks may be avoided by the proper treatment. The successful treatment of the attack alone is not enough, but the future of the child must be safeguarded from a repetition of the seizure, and the possible development of a cerebral habit, leading to epilepsy.

Epidemic Catarrhal Jaundice.—Leonard Guthrie (*British Jour. Child. Dis.*, 1913, x, 1) reports a small epidemic of catarrhal jaundice in children. There were 10 cases in all, and they occurred during a period of three months. Eight cases were in contiguous districts. The children were aged from three to eleven years. In 3 instances more than one member of the same family were affected. In one family two sisters, in another two sisters and one brother, and in a third a brother and sister became jaundiced between a fortnight to three months of each other. The remaining 3 cases were sporadic. All the cases showed deep jaundice, clay colored stools, and bilirubinuria. The onset was accompanied by malaise, languor, and slight fever (99° to 100° F.). In several cases vomiting occurred. The duration was from three to four weeks. Bradycardia was not observed. The liver was enlarged in 6 cases and greatly so in 4, in which it extended to within one inch of the umbilicus. The liver began to subside in size on the appearance of bile in the stools, and regained the normal size in from one to two weeks. None of the patients were seriously ill at any time. The condition is probably caused by some common organism capable of giving rise to infective hepatitis. Blockage of the main duct by mechanical causes does not produce so great an enlargement of the liver as occurred in these cases. The influenza bacillus has been designated by some as the cause of the condition. Cockayne refers to the possible analogy with mumps and the metastatic swelling of the testes and pancreas, and there is a possibility that mumps, acute pancreatitis, and hepatitis may be allotropic forms of the same infection.

Tuberculosis in Children.—Eric Pritchard (*Practitioner*, 1913, xc, 280), in an article on tuberculosis in children, states that it is the commonest of all diseases affecting childhood. The incidence rate rises from zero at birth to 90 per cent. at the age of fourteen years.

Children, although highly susceptible, are little liable to fatal results except during the first two years of life. The mode of infection is mostly from human sources, by direct contact, or air-born. Unboiled, contaminated cow's milk probably causes the smaller percentage of infection of the bovine type. It is a disease especially of the lymphatic system in children, and this accounts for the absence of constitutional symptoms in many cases. Enlargement of the mediastinal glands is found in 88 per cent. of all tuberculous cases coming to autopsy. Among other diagnostic signs indicating enlarged mediastinal glands, Pritchard mentions spasmodic cough without expectoration or obvious cause, and impairment of resonance to the right of the sternum at the second intercostal space. The diagnosis of the general condition rests on the consideration of the constitutional symptoms, specific tests as the von Pirquet or Moro, and investigation of the lymphatic system. The treatment is prophylactic during the first two years of life, and the maintenance of strength during the later years of childhood. Infants should be removed from an environment of open infection. Employment of the graduated cold bath, from 100° F. down to cool, and a varied and liberal proteid diet with supplemental feeding of raw beef-juice, yolk of egg, plasmon, etc., are of great value. Later in childhood it is highly important to support the strength during the debility following measles, pertussis, and chickenpox, and to remove the child to the country if possible. In treating established cases the tuberculin treatment is uncalled for in the majority of cases. It is probably of value in surface or surgical affections. The hygienic and medical treatment is best. Intestinal stasis is decidedly unfavorable to tuberculous children. Pritchard uses an emulsion of petroleum, dram j to ij, with liquor pancreatis, ℿx, and calcium hypophosphite, gr. j, three times a day, for intestinal stasis. He also prefers giving calx. sulphurata for involvement of the glands of the neck, syrup of the iodide of iron for plastic infiltration and general debility, and creosote, preferably in cod-liver oil, in all pulmonary and advanced cases.

The Leukocytes at Different Age Periods.—Dina Rabinowitsch (*Archiv f. Kinderheilkunde*, 1912, lix, 161) refers to the observation on the leukocytes in children by various investigators, most of whom agree that the total white-cell count is higher during the first three years of life than in the adult, and that the lymphocytes are much more numerous, and the neutrophiles less in number during this period than in the adult. An adjustment takes place in the number of cells of the above type until at the fifteenth year the numbers approach the adult differential count. In Carstanjen's figures from the sixth month to the fifth year the lymphocytes drop from 50 to 25 per cent., the transitional forms from 10.5 to 7.2 per cent., and the neutrophiles rise from 35.5 to 61 per cent. From the fifth to the fifteenth year Carstanjen notes very little change in the percentages. The findings of the various investigators differ in their differential counts and in the age periods in which the different cells vary in number. Rabinowitsch, therefore, made a study of the blood in 150 healthy children to determine the differential count of the leukocytes at varying ages. The total count of white cells in children aged from

one to fifteen years, except those in the first year, showed practically the same number as in adult life, or about 6000 to 7000 cells. Sex made no difference in the count. Polynuclear neutrophiles increased in number with the age of the child from 30 per cent. at the first year to 70 per cent. at the fifteenth or sixteenth year. Lymphocytes showed 60 per cent. of all white cells at the first and second year, and gradually decreased with age until they reached 30 per cent. at the sixteenth year. Eosinophiles averaged from 4 to 6 per cent. throughout, varying considerably in some children at the same age period. Transitional forms averaged throughout from 2 to 3 per cent. Mast cells averaged from 0.3 to 0.6 per cent., and were often absent altogether. Large mononuclear cells averaged from 1 to 3.3 per cent., and were practically the same for all ages of children.

OBSTETRICS

UNDER THE CHARGE OF

EDWARD P. DAVIS, A.M., M.D.,

PROFESSOR OF OBSTETRICS IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA.

Operation for Puerperal Septic Infection.—At the recent International Congress of Obstetrics and Gynecology, Berlin, September 9, 1912, KOBLANCK, of Berlin, read a paper in which he advocated surgical treatment of puerperal sepsis in cases where the infection became localized. It is often difficult to diagnosticate the location of the infection. In 44 cases of general peritonitis he had operated, and in 23 he abstained from operation. Among the 44 cases 9 recovered and 35 perished. In 15 hemolytic bacteria were found, and among these were 4 recoveries. In the second series of 23 not operated upon, 22 died, and 1 recovered. In selecting the time for operation, in 11 patients between the first and third day was chosen, and of these 3 recovered and 8 died. In 14, operation was done from the fourth to the sixth day, with 3 recoveries and 11 deaths. In 8, from the seventh to the ninth day was chosen, with 2 recoveries and 6 deaths. When the patient had been ill from ten to twenty days, there were 11 cases operated upon, with no recoveries and 11 deaths. This would indicate that the sooner operation is performed after a diagnosis can be made, the better. In 72 cases, the principle infective focus was extirpated. Among these were 11 extirpations of the uterus, with 3 recoveries and 8 deaths. Among these patients 5 had hemolytic bacteria, with 1 recovery. Extirpation of the adnexa was practised 8 times, with 5 recoveries and 3 deaths. Hemolytic bacteria were found in 4 patients, of whom 3 recovered. Metastatic abscess was operated upon 35 times, empyema 8, with 1 recovery; joint abscess 9, with 7 recoveries; abscess of the skin and muscle 18, with 13 recoveries. Extirpation of septic veins was practised 17 times; simple ligature 7 times, with 4 recoveries and 3 deaths, of whom 3 had hemolytic bac-

teria, and 2 recovered; and 10 resections of veins, with 3 recoveries and 7 deaths, of whom 8 had hemolytic bacteria, with 3 recoveries. This resection of veins was accompanied by the extirpation of the uterus and adnexa. There were 36 cases of abscesss of the parametrium, with 34 recoveries and 2 deaths; hemolytic bacteria, 8, with 7 recoveries; and 5 cases of circumscribed peritonitis, with 2 recoveries and 3 deaths, 3 having hemolytic bacteria, with 2 recoveries. His experience would indicate that septic peritonitis should be operated upon at the earliest possible moment, and that extensive operation on the genital organ is indicated in metastatic infection. The septic uterus should be removed through the abdomen. The results will be improved if operation is performed sooner.

The Influence of the Age of the Mother on the Sex of the Child.—AHLFELD (*Monatschr. f. Geburtsh. u. Gynäk.*, 1912, Band lxxxvi, Heft 3) concludes from his investigations that the number of male children is greater than female children in those women in whom the birth of the first child occurs after the average age. While he personally is satisfied that this is accurate, he thinks it should be corroborated by further investigation.

The Topography of the Umbilicus in Mothers and Newborn Infants.—KAKUSCHIN (*Monatschr. f. Geburtsh. u. Gynäk.*, 1912, xxxvi, Heft 3) has investigated the relative topography of the umbilicus in the newborn child and in the mother. He finds that in taking measurements from the sternum to the umbilicus, from the symphysis to the umbilicus, and from the anterior superior spine of the ilium to the umbilicus, in different individuals, that differences as great as 14 cm. are found. Women above the average age, who have not borne children have greater measurements than the average of younger women. The occurrence of childbirth does not seem to influence these measurements. During pregnancy the lower portion of the abdominal wall is greatly distended, and all measurements in multiparæ are much greater than in primiparæ. During pregnancy the greatest increase is found in the measurement from the left anterior superior spines of the ilium to the umbilicus. As the length of the trunk of the mother's body increases, the measurement from the umbilicus to the pubis is greater. In the first day after labor the measurement from the xyphoid cartilage to the symphysis grows shorter, so that it is below its average measurement in a young woman. The greater the weight of the newborn child the higher is the umbilicus in relation to the length of the body. In female children the umbilicus is relatively higher than in male children. In full term children born in breech presentation, the umbilicus is relatively higher in the body than in children born in vertex presentation.

Perforation of the Uterus following Abortion.—PUPPE (*Monatschr. f. Geburtsh. u. Gynäk.*, 1912, Band xxxvi, Heft 3) describes 2 typical cases illustrating the danger which the general practitioner often incurs in attempting to deal with septic abortion. The first patient was the mother of nine living children, who had interrupted menstruation, and was troubled with cough and chest symptoms, for which she

consulted a general practitioner. Afterward there developed a foul discharge from the vagina, for which the doctor applied a tampon. He afterward examined the patient under an anesthetic, finding the cervix slightly dilated, so that Hegar's dilators were used to open the canal. When the dilator No. 14 was introduced, some hemorrhage followed which was checked by a tampon and was supposed to come from the mucous membrane of the surface. The putrid mass was removed so far as possible from the uterus, and the patient was sent from the consulting room to her lodging. She shortly afterward died from peritonitis. On examination a large perforation in the left parametrium was present, and behind the left ovary the peritoneum had been extensively wounded. There was a small piece of placenta in the cervix. The second case was that of a woman who had borne three children, who becoming pregnant again, endeavored to interrupt the pregnancy by hot baths, and probably interference. Hemorrhage finally developed, with pain over the sacrum, and gradual impairment of health. The patient consulted a physician, who made an examination and attempted to empty the uterus by the finger. Failing this, he used a curette and placental forceps. He then irrigated the uterus with a uterine catheter. It was observed that the water used in the irrigation did not entirely return. The patient went in a cab from the doctor's office to her house. She soon after died from peritonitis. On section, the uterus had been perforated at the fundus near the insertion of the left tube. These cases draw attention to the familiar fact that in the presence of septic abortion curetting is exceedingly dangerous. Such patients should be immediately transported to hospital where, under anesthesia, they should be carefully examined. The cervix should be dilated with the finger, and if the body of the uterus is firm, the finger or a large blunt-edged curette may be carefully employed, followed by gentle irrigation and by a tampon of iodoform gauze. If the body of the uterus is soft, nothing should be introduced within its cavity. In preparing to empty the uterus, preparations should also be made for abdominal section, and if the operator fears that he has perforated the womb during his examination, the abdomen should be immediately opened. In all doubtful cases the interior of the womb should not be molested.

An Early Case of Chorio-epithelioma Uteri.—THOMPSON and STEWART (*Jour. Obst. and Gynec. British Empire*, September, 1912) report from the Leeds Infirmary the interesting case of a multipara, aged forty-five years, who had bleeding from the uterus after six weeks' amenorrhea. This continued for ten days, obliging the patient to remain in bed. A few weeks after the first hemorrhage a second one occurred during a journey, which obliged the patient to interrupt her journey, and caused her to be very anemic upon her arrival home. On examination, small pieces of vesicular mole were found in a blood clot which had passed from the vagina. The patient was very anemic, with high temperature, and offensive vaginal discharge. The uterus was enlarged, corresponding to the period of pregnancy. After curetting, the interior of the uterus felt smooth. The materials removed were vesicular mole, portions of placenta, and blood clot. Five weeks afterward the patient bled so profusely that

death seemed threatened. On examination, a spongy mass was adherent to the posterior wall of the uterus. It was thought best to remove the uterus by abdominal hysterectomy, and this was done without complications. Fourteen months after the operation the patient was in good health and free from signs of recurrence. On examining the uterus it was three times the normal size. On the posterior wall near the fundus was a soft, friable mass, in the centre of which was a shaggy growth the size of a small walnut, infiltrating the uterine muscle. The remainder of the uterine cavity was smooth. The ovaries were considerably enlarged with numerous cysts. On microscopic examination the characteristic appearance of chorioepithelioma was present. The uterine veins were invaded not more than one-half through the uterine wall, and but one necrotic villus was present. In the tumor there was a striking preponderance of intermediate or wandering cells, with comparatively little syncytium and Langhans' cells. Masses of the latter, however, were found in the sinuses, which is considered evidence of malignancy. Both ovaries were the seat of lutein cyst formation.

GYNECOLOGY

UNDER THE CHARGE OF

JOHN G. CLARK, M.D.,

PROFESSOR OF GYNECOLOGY IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA.

Fascial Transplantation in Vesicovaginal Fistula.—A novel method has been resorted to by SCHMID (*Zeitschr. f. gyn. Urologie*, 1913, iv, 33) in the treatment of a stubborn case of vesicovaginal fistula following a Wertheim operation for carcinoma of the uterus. The patient was aged forty-three years; the bladder was injured during the operation, and was repaired, but a large fistula resulted, which two subsequent operations failed to close. At the third attempt, Schmidt, after again freshening the edges and closing the vesical mucosa in a transverse line with catgut, inserted between the vesical and vaginal walls a rectangular piece of fascia, about 3 by 2 cm., taken from the fascia lata of the right thigh. It was fastened with one catgut suture at each corner in such a manner as completely to cover the line of suture in the bladder wall; the vaginal mucosa was then closed over it with silk in a vertical direction. On examination of the patient three months later there was found to be no leakage whatever, and good vesical control. A thickening could be felt in the anterior vaginal wall, and by cystoscopic examination a slight protuberance could be seen on the posterior wall of the bladder, reaching not quite to the interureteric fold, and evidently corresponding to the fascial flap. The mucosa was smoothly healed over this, but showed a certain amount of hyperemia in the neighborhood of the scar. Schmidt admits that the third operation might possibly have cured this case, even without the use of

a fascial transplant, but he does not think it likely, as the tissue surrounding the fistula was densely indurated, and would in all probability have retracted as in the other attempts. There is no difficulty associated with the technique of transplanting such a small piece of fascia, which is almost sure to heal well, and which certainly, in Schmidt's opinion, gives valuable extra support in cases such as the one cited.

Menstrual Disturbances of Tuberculous Origin.—The menstrual disturbances which often accompany tuberculosis, and which have usually been attributed to the consequent anemia or cachexia, are really, according to Hollós (*Deutsch. med. Woch.*, 1912, xxxviii, 2407), toxic phenomena, *i. e.*, specific manifestations of the tuberculous virus localized somewhere in the body. He thinks that an unusually early or an unusually late onset of menstruation (before the eleventh, or after the sixteenth year) is very suggestive of tuberculosis; when tuberculosis is acquired after menstruation has been established, its toxic influence is often manifested by irregularities, amenorrhea, or dysmenorrhea. Hollós thinks that these toxic phenomena stand in some relation to the degree of immunity possessed by the individual, and to the power of reaction to a given source of intoxication, basing this belief on his experience that these toxic symptoms are absent in a much larger percentage of prognostically unfavorable cases than of cases with a good prognosis, and also on his observation that the menstrual disturbances not infrequently disappear after specific treatment of the tuberculosis.

Ovarian Involvement in Epidemic Parotitis.—In contradistinction to the testicle, which, as is well known, is exceedingly frequently the seat of a metastatic infectious process in cases of mumps, very seldom has similar involvement been demonstrated in the ovary, and 2 such instances reported by Brooks (*Jour. Amer. Med. Assoc.*, 1913, lx, 359) are therefore of interest. Both patients were multipara, aged twenty-eight and twenty-four years respectively; in the first case the parotid involvement was unilateral and comparatively slight, but accompanied by a temperature of 104°. Seven days after its onset the ovary of the same side became enlarged, very painful, and tender on examination; the symptoms subsided after a couple of days, but the next menstrual period came on ten days ahead of time, and was more profuse than normal. In the second case the parotid involvement was bilateral, and was followed in five days by very severe pelvic pain on both sides. On examination both ovaries were found enlarged to the size of large eggs, and extremely tender. Two days after this, an acute mastitis supervened, affecting both breasts, but soon subsided, as did the ovarian inflammation. Both these patients have been under observation for a period of five years or over since their attack, and in neither instance has pregnancy occurred during this time. Brooks believes that while the condition is decidedly uncommon, it probably occurs more frequently than is generally supposed, as unless the symptoms are very marked, as in the cases he reports, it is not thought of or examined for. The probable reason for the infrequency of ovarian involvement as compared with that of the testicle is that the latter is much more exposed to slight trauma, which

favors the localization of secondary infection. Judging from these cases, and the comparatively few to be found in the literature, the involvement of the ovary appears to be a benign process, undergoing spontaneous cure, though at times associated with temporary menstrual disturbances.

Differential Diagnosis Between Ascites and Ovarian Cysts.—A simple method of clearing up the diagnosis in cases of doubt between ascites or a relaxed ovarian cyst is described by DIENST (*Münch. med. Woch.*, 1912, lix, 2731). He recommends it especially to the attention of general practitioners who may under these circumstances be forced to tap in order to relieve threatening pressure symptoms, or because of the patient's refusal of exploratory operation. The test is based upon the fact that ascitic fluid always contains fibrinogen, which is precipitated by common salt, whereas this is never found in the contents of ovarian cysts. If, therefore, a small quantity of the fluid removed at the tapping is placed in a test-tube, and one-third its volume of salt added, a flocculent precipitate will form on standing, after the salt has dissolved, if the fluid is ascitic in origin. If no precipitate forms, the fluid is certainly not ascitic, and exploratory operation should be insisted on. Dienst thinks that this test has a distinct field of usefulness, for in not a few cases of ovarian cyst, the contained fluid presents all the appearances of that from an ascites, and *vice versa*, in some cases of ascites with admixture of chyle, the fluid may strongly suggest rather thin cyst-contents.

Relation of Corpus Luteum Formation to Menstruation.—In a paper published about a year ago, and reviewed in this department at that time, Fraenkel stated his belief, based on clinical observation during laparotomies, that corpus luteum formation occurs in the intermenstruum, and chiefly in the second half of this period, so that while ovulation and menstruation do not occur simultaneously, they have a direct time-relation to each other. These clinical observations have been completely confirmed by histologic studies made by MEYER and RUGE (*Zentralbl. f. Gynäk.*, 1913, xxxvi, 50) on 87 ovaries removed during hysterectomies. By comparing the ovarian findings with the menstrual histories of the patients, and with the histologic appearance of the endometrium of the corresponding uteri, Meyer and Ruge have determined that the stage of proliferation begins about eight to twelve days after the preceeding menstruation, the stage of vascularization about the fourteenth day, and that practically complete development of the corpus luteum is reached by the seventeenth day, although the cells continue to undergo some slight further increase in size up to one or two days before the beginning of the next menstruation. Involution then begins, and by the eighth day after the menstrual period—*i. e.*, by the time the new corpus luteum is ready to start development—the old one has become completely functionless, but its complete involution to a corpus albicans, with loss of all lutein cells, takes a much longer time, so that five or six degenerating corpora lutea are often found in one ovary. In case pregnancy occurs, however, the corpus luteum remains at the height of its development throughout, and by the second month can be distinguished from that of menstruation by the rich plication of the cell layer and the extensive develop-

ment of connective tissue. The actual time of follicle rupture has not as yet been determined with accuracy, but it probably occurs immediately, or at least very shortly after menstruation, which time should therefore be the most favorable for impregnation, and which usually corresponds with a period of increased *libido sexualis*.

OTOLOGY

UNDER THE CHARGE OF
CLARENCE J. BLAKE, M.D.,
PROFESSOR OF OTOLOGY IN THE HARVARD MEDICAL SCHOOL, BOSTON.

A Case of Gonorrheal Perichondritis of Both Auricles.—H. FISCHER (*Zeitschr. f. Ohrenheilkunde*, lxvi, 1–2). This unusual demonstration of gonorrheal infection as cited by Fischer was exhibited after three attacks of increasing severity as to their manifestations in a man, aged twenty-two years. The first infection, in 1906 resolved spontaneously in between eight and nine weeks without complications. The second infection, in 1907, was followed, eight days later, by painful swelling of both ankles and the right knee. The third infection, in 1909, had similarly painful consequences involving also the right wrist, shoulder, and sternoclavicular articulation, as well as several finger joints. In addition there was a sudden excess of burning and itching sensations in both auricles lasting several days, and followed by a swelling, especially pronounced at the periphery, and accompanied by circumscribed nodulated tumefactions; the auricles felt hard and thick, and were intensely painful. There was no treatment and the acute symptoms subsided in ten weeks, leaving only a moderate degree of swelling. In November, 1911, another infection, untreated because the patient was at sea, followed two weeks later by painful swelling of the auricles, and in December the case came under immediate observation and treatment which resulted, at the end of a month in relief from the acute articular symptoms, and the temperature became normal. Ten days later there was a sudden rise in the morning temperature without evidence of recurrence of articular irritation, but with a repetition, at the end of three days, of the burning and itching sensations in the auricles which had been the preliminary symptoms of the perichrondritis of three years previously. In twenty-four hours both auricles had become red and swollen, especially at the periphery, and tense to the touch, which caused severe pain. In addition to the general swelling of the auricles there were on the antihelix and at the back of the outer edge, two hard purplish nodules, firm, resistant, and unfluctuating, and especially tender. Two and one-half months later the general swelling and the nodules had much decreased, but were still in evidence. The implication of the auricle in this unusual case was plainly not a dermatitis, but an inflammation of the cartilage and of the membrane, and while the local presence of gonococci was wanting, both the character of the inflammatory process, its resemblance to reported cases of perichondritis in other parts

of the body in which the exciting cause was demonstrable and the relationships of the auricular manifestation to the more severe infections, in this individual case are in favor of the inferential diagnosis.

Contributions to the Study of the Bacteriology of Acute Otitis Media Purulenta.—In the cases reported in this communication, ABERT (*Archiv f. Ohrenheilkunde* lxxxv, 251) took, for the purposes of his investigation, pus taken from the surgically opened mastoid process, in the course of the operation, not from the middle ear through the medium of the external canal, in which respect his investigation differs from many others with which the results may be compared. A bacteriological examination was made in 110 cases and, in the majority, over 90 per cent. streptococci were present, in 18 cases streptococcus alone, 19 cases almost entirely streptococcus, 73 cases of mixed infection, streptococcus in preponderance, and also saprophytes, staphylococcus, and pneumococcus. Of these 73 cases streptococcus mucosus was determined in 8 cases, in 2 cases a pure culture, 2 cases staphylococci only, and 2 cases in combination with pneumococcus; there were also 2 notable cases in which only saprophytes were found. Of the infectious diseases, in which suppurative inflammation of the middle ear is a not infrequent sequence, scarlet fever stands first, and the bacteriological examination of the observed cases gave the following result: Streptococcus in pure culture, 5; streptococcus almost entirely, 4; streptococcus mucosus, 2; streptococcus and staphylococcus, 4. The aural implication in measles was much less frequent and bacteriologically was as follows: Streptococcus in pure culture, 1; streptococcus mucosus, 1; streptococcus and rod-like bodies, 1; staphylococcus albus, 1. Of secondary otitis there were 2 cases, one following diphtheria, the other in the course of a tuberculous infection in both of which the bacteriological finding gave streptococcus and staphylococcus. There were, in addition, 6 cases of middle-ear inflammation following influenza which could not definitely be called the otitis of influenza because no influenza bacilli were determined. Burkner reports 4 cases of otitis following influenza in which careful bacteriological examination of the secretions from the middle ear were made without proving the influenza bacillus, but demonstrating in 2 cases streptococcus pyocyaneus, in 1 case streptococcus mucosus, and in the remaining case pneumococcus. From the cases cited it was evident that the streptococcus infection preponderated, the streptococcus mucosus coming next. Next in frequency were the saprophytes, and with them a rod-like body, both aërobic and anaërobic in culture closely resembling the pyocyaneus. The saprophytes were frequently associated with bacteria, streptococcus, staphylococcus, and pneumococcus, but the exact procedure in effect of these mixed infections is not yet determined, the influenza otitis is not solely referable to influenza but may be induced by other agents.

Conditions Causing Permanency and Cicatricial Closure of Perforations of the Drum-head in Childhood.—Perforations of the drum-head have a tendency to heal because of the histological structure of that compound membrane and the conditions which lead to a permanent opening are, therefore, according to B. GOMPERS (*Zeitschr. f. Kinderheilkunde*, v, No. 1), especially worthy of consideration. In

the first year of infancy large perforations of the drum-head are rarely seen, and then only in cases of lowered vitality, in hereditary syphilis, or advanced tuberculosis; occasionally large perforations are observed in cases of measles. In the second year extensive destruction of the drum-head is observed in cases of scarlet fever, and, less frequently, in cases of typhus and measles. The extent of the destruction is limited by the vital resistance, the conditions unfavorable to healing being, according to the observations of Gompers, physical impoverishment of the parents at time of procreation as a consequence of poverty, drunkenness, syphilis, diabetes, and, especially, tuberculosis. The children of such parents have poorly nourished tissues of moderate resistance and minimum power of regeneration, and in these cases are found not only extensive persistent perforations of the drum-head, but also necrotic processes in the neighboring bony structures, and continuance of the middle-ear suppuration in the chronic form. With betterment of the general condition, accompanying appropriate aural treatment, the suppurative process may be checked and even large perforations conglutinated, but with a lowering of the general condition in strength and vitality the destructive process in the drum-head continues. In the spontaneous closure of perforations, by cicatricial tissue, the inflammation which was the cause of destruction furnishes the irritative incentive to the formation of new tissue; if this inflammatory reaction is wanting, however, the perforation remains constant until a further inflammatory reaction again stimulates newgrowth; in one case a large and long persistent perforation was observed to have become closed, as the result of a new inflammation of the middle ear, consequent upon an influx of cold water. Closure of perforations of the drum-head may be induced by the application of irritating substances to the edges of the perforation but the still more valuable preventive measure in acute inflammations of the middle ear, is an early paracentesis.

Hemorrhage Accompanying Paracentesis of the Drum-head.—Paracentesis of the drum-head in cases of acute congestion of the middle ear, CARL LUDERS (*Zeitschr. f. Ohrenheilkunde*, lxvi, 1–2) says, is accompanied by hemorrhage varying in degrees proportionate to the degree of congestion and the extent and location of the incision, but usually occurring spontaneously, or easily checked by moderate tamponage. When the hemorrhage is so severe as to instantly fill, and then continue to flow from the external canal, the possibility of a complication is immediately suggested, either in the form of a structural abnormality or in a constitutionally predisposing cause. In the latter instance the outflow of blood from the middle-ear immediately following the paracentesis, instead of slackening within a few seconds, continues undiminished to the extent even of extruding the attempted tamponage of the external canal, or exhibiting itself as an outflow from the nose and mouth of the blood passing from the middle ear through the channel of the tympanopharyngeal tube. The structural abnormalities contributing to the possibilities of excessive bleeding from a paracentesis are those in which the internal carotid and the jugular bulb encroach upon the lumen of the tympanum; the constitutional predisposing causes are to be found, for example, in the natural bleeders, the nephritics, and the diabetics.

Following the report of individual cases, in one of which the recurrent hemorrhages led to operation with a lethal sequence, and a review of the literature of the subject Luders draws the following conclusions: (1) In constitutional and infectious diseases the hemorrhage following a paracentesis of the drum-head may much exceed the average of the same result in uncomplicated acute congestion of the middle ear. (2) Considerable and dangerous bleeding from the ear as a consequence of paracentesis of the drum-head is exceedingly rare. Of the thousands of cases of paracentesis there are, in the literature of the subject, in addition to the 2 cases cited by Luders, but 6 others on record. (3) In all of the recorded cases of excessive hemorrhage, following paracentesis, the blood comes from the jugular bulb and not from the carotid. (4) Alteration from the ordinary procedure in paracentesis or discrimination as to the location is not indicated. (5) A considerable hemorrhage as a consequence of a paracentesis is less dangerous in itself than is the opening of a large bloodvessel into a suppurative cavity; the consequent pyemia occurred in 2 out of the 8 cases cited. The second of the 2 cases, cited by Luders, is the only one reported in which recurrent hemorrhages led to the necessity for operation, the experience in this case indicating the necessity for ligation in the case of excessive hemorrhage following paracentesis.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

JOHN McCRAE, M.D., M.R.C.P.,

LECTURER ON PATHOLOGY AND CLINICAL MEDICINE, MC GILL UNIVERSITY, MONTREAL; SOME TIME PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF VERMONT, BURLINGTON, VERMONT; SENIOR ASSISTANT PHYSICIAN, ROYAL VICTORIA HOSPITAL, MONTREAL.

The Specific Treatment of Experimental Pneumococcus Meningitis.—LAMAR (*Jour. Exp. Med.*, November 1, 1912), publishes the results of experimentation with a promising therapeutic measure, namely, the use of a mixture of socium oleate, boric acid, and antiserum. It is well-known that the use of anti-pneumococcus serum alone has been disappointing, the extent of its efficacy being confined within a very short space of time, and depending apparently upon the homologous serum being employed. With regard to the mixture spoken of above, Lamar promises an early statement as to whether homologous antiserum is absolutely necessary or not. In any case the number of strains of pneumococci is not a large one, and a suitable polyvalent serum if necessary may be procurable for use. In stating his conclusions Lamar points out that virulent pneumococci injected into the cranial or spinal cavities of monkeys produced a rapidly fatal meningitis very similar to that seen in man. Homologous immune serum, if used early, may prevent infection, or may retard the course of the disease, but subsequently is powerless to save life. The mixture of sodium oleate, immune serum and boric acid, administered repeatedly

did, however, arrest infection that had already gained headway, and led to full recovery. Such a mixture is valuable not only for meningitis but also for other pneumococcic infections such as those of the joints or the serous cavities.

The Detection of Anthrax Spores in Industrial Material.—Glynn and Lewis (*Jour. of Hygiene*, June, 1912) publish the results of their work, in Liverpool, upon industrial material suspected of harboring anthrax. They were successful in more than 20 per cent. of the samples in a large series, and further they were successful in finding spores in samples disinfected by the methods now in vogue, which indicate that these methods are as yet imperfect. Glynn and Lewis consider it practically impossible to completely sterilize certain industrial materials without damaging them, but they consider that the present imperfect method is much better than none at all. In the last five year period, the British Islands show 366 human cases of which 81 were fatal, with a steady increase in the number of cases developing in the agricultural community, due to the moderate but steady increase of the disease among domestic animals in the same period. The materials usually submitted for investigation are hides, wool, hair, and bones, and importations from the Malay States gave Glynn and Lewis most of their successful results. The methods usually employed in the detection of the spores are agar plate cultures or the inoculation of guinea-pigs, of which the latter is favored.. Inoculations should be made in duplicate with the centrifuged deposit of watery extract, and it is a disadvantage at present insurmountable that a considerable number of animals die from the effects of pathogenic anaërobes.

Pseudoleukemia.—At the latest meeting of the German Pathological Association, a conference was devoted to so-called pseudoleukemia (*Verhandl. d. deutsch. path. Gesellsch.*, 1912), better known in our literature as Hodgkin's disease. Fraenkel, of Hamburg, referred to the original conception of Cohnheim, and showed that in these cases there was anemia, and a relative lymphocytosis, which lymphocytosis may pass over into a definite leukemic state, and that this happens oftener than is thought. In fact, Fraenkel says, in the few cases he has sectioned, he found a true leukemic state; this he thinks may have arisen but a few days or even hours before death, in that the organs were deprived of the ability to hold back the white cells, which then came into the circulation and gave the picture of leukemia. Although the changes in pseudoleukemia are usually observable in peripheral groups of nodes, yet internal groups can also be discovered to show microscopic changes. The enlargement of the spleen, similar to that seen in leukemia, is notable, and when this is very great, Fraenkel thinks it is hardly right to call the disease pseudoleukemia, since even in cases without splenic enlargement the increasing lymphocytes can be seen in the follicles. In the definition of the disease one has to admit the impossibility of making a classification according to the groups of nodes involved, as practically any group may be affected. Further, there may be the appearance of localized masses in the liver, kidney, lung, bowel, and elsewhere, and even in the skin as lymphodermia cutis. All this is not in any sense metastatic extension. Pseudoleukemia is a systemic disease of the lymphatic tissue of the entire

organism; variation of intensity and of site produce the varying pictures. Fraenkel rules out the cases of Mikulicz, who described symmetrical swelling of lachrymal and salivary glands as an early stage of pseudoleukemia; rather are these to be considered as an atypical tuberculosis. Similarly, he would rule out infantile status lymphaticus. To distinguish lymphosarcoma, however, is quite another matter; in fact, Fraenkel takes the stand of Virchow that lymphosarcoma and pseudoleukemia stand very close to one another. Chloroma, Fraenkel would designate as lymphatic chloroleukemia, or if the blood remains aleukemic, hyperplastic chloropseudoleukemia; not in any sense does he consider it as a true neoplastic state. Myeloma he would class as a medullary localization of pseudoleukemia; myeloma has thus no actual identity with true tumor formation. There must therefore be two forms of pseudoleukemia, the ordinarily observed lymphoid forms and the much rarer myeloid forms—a generalized, intra- and extra-medullary hyperplasia of myeloid tissue, connected with an unchanged, or not definitely leukemic blood state. Fraenkel is unwilling to admit a splenic form of myeloid pseudoleukemia. STERNBERG, of Brünn, stated at the outset, that Hodgkin's cases were of so variable a nature that we have there no secure basis for a definition of pseudoleukemia. Having dealt with a large number of diseases which have little connection with true pseudoleukemia, he comes to the question of lymphosarcoma in Kundrat's sense of the word, which he considers must be admitted to have some connection with pseudoleukemia; at least, that form of it known as hyperplastic lymphoma is to be differentiated from true sarcoma, and both it and pseudoleukemia possess in common an alteration of the general body constitution. The frequently observed generalized lymphoid hyperplasia existing in tuberculous infections, although similar to the picture of pseudoleukemia, Sternberg characterizes as a purely tuberculous phenomenon. He counts that pseudoleukemia should not be considered in any way as an early stage of lympholeukemia, or of lymphosarcomatosis, but nevertheless feels that actually it is the same process as exists in lymphatic leukemia, and it is to be distinguished from the same only if the escape of the lymphocytes into the blood stream is restrained. Sternberg would thus admit an acute generalized pseudoleukemia, and a localized pseudoleukemia, which again may be splenic or medullary, and this last not in the unlimited sense which sould include Banti's disease, but merely in the restricted sense of Cohnheim and Wunderlich. In short, Sternberg groups into pseudoleukemia, lymphosarcomatosis (with the restriction that the metastases must be in the lymphoid tissue), lymphogranulomas, the multiple plasmomas, and the splenomegalies, in all of which there is a more or less universal hyperplasia of the lymphoid tissue without leukemic signs in the blood. In discussion BENDA considered that fuller clinical examination would prove that the cases of so-called pseudoleukemia in which at autopsy the blood shows leukemic signs had been insufficiently examined clinically, and he quoted a case in which diagnosis of Banti's disease had led to extirpation of the spleen and subsequent death, because the recessions of the leukemic state had not been recognized. HIRSCHFELD considers that lymphogranulomatosis would be a preferable term to pseudoleukemia. In further discussion Aschoff thought that the term pseudoleukemia should be left to clinicians, and the

pathologists should use the term aleukemic or proleukemic lymphadenia or lymphadenosis. If we were to sum up the prevailing views of the members of the Association upon the causation of hyperplasia of the lymphoid tissues, it seems to be that a certain number of the cases are definitely due to tubercle bacilli; that in a fair number of other cases Much's granules have been discoved, which may be considered as evidence of the presence of tubercle bacilli of some variety, probably of reduced virulence; that even where tubercle bacilli and Much's granules have not been found there may yet be some cases caused by the virus of tuberculosis. Definite evidence is now at hand that in cases where Much's granules have been found and injection made, the animals so subjected have succumbed to a low grade tuberculosis. With regard to the terminology, Aschoff's suggestion of lymphadenosis seems a very good one, and it is possible to modify such a term with the adjective aleukemic or leukemic, according to the accompanying circumstances.

Diurnal Filaria.—Through the daily press comes the information that the metamorphosis of Filaria loa has been discovered to occur in the salivary glands of a fly belonging to the genus Chrysops. The information comes by cablegram from DR. R. P. LEIPER, who is at Calabar, and this mode of transmission of news suggests the fear of supersession which has invaded even laboratories. Filaria loa is confined to the west coast of Africa, and its embryos are found in the blood only during the day-time, in contradistinction to those of Filaria bancrofti, which are found only during the night. Not a fatal disease, the infection by Filaria loa is common in West Africa, its best known manifestation being the so-called "Calabar swelling" which is due to the presence of the worm in the muscles and in the vicinity of the tendons, where painful swellings are set up which may interfere seriously with the function of the limb concerned. In connection with the habits of the embryos of Filaria loa it is interesting to note that the insect concerned is one which bites by day, suggesting a parallel with the mosquito, which is responsible for the transmission of Filaria bancrofti, and which bites at night.

The attention of subscribers is called to the fact that the article entitled "Tuberculin Therapy in Surgical Tuberculosis," by Thomas Wood Hastings, M.D., which appeared in the issues of this Journal for August and September, 1912, was a Mütter Lecture delivered before the College of Physicians of Philadelphia on December 9, 1910.

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All communications should be addressed to—

DR. GEORGE MORRIS PIERSOL, 1927 Chestnut St., Phila., Pa., U. S. A.

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